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THE EFFECT OF SURGICAL OPERATIONS ON THE LEVEL OF CEVITAMIC ACID IN THE BLOOD PLASMA*

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IN THE fall of 1937 an extensive study of cevitamic acid in relation to the healing of surgical wounds was started. It is expected that reports on other phases of this work will be published shortly. Early in the work it was seen that if blood specimens for cevitamic acid determinations were taken shortly after operation, extremely low values in the blood were the rule. It was therefore decided to study the effect of surgical procedures on the blood level of this vitamin intensively by determining the level before and several times after operations on many patients. No conclusive studies of exactly this nature have been found in a careful search of the literature, but there are four papers which deal in some fashion with the subject, and a fifth that has a direct bearing on it but contains only fragmentary data.

In 1937 Lauber, Bersin and Nafziger[1] found that the urinary output of ascorbic acid in healthy rabbits was increased after general or local anesthesia and after operations. They concluded that these findings pointed out the importance of maintaining or establishing a vitamin C reserve before an operation. Later in 1937, Lauber[2] studied the same subject in rabbits injected with excessive doses of 100 mg. of cevitamic acid daily until their urinary excretion reached a constant level. In these animals, after anesthesia with ether, chloroform or ethyl chloride, the output of the acid sank very low for one day but promptly rose again. However, after Evipal anesthesia the rise was delayed and the level of excretion remained low for several days. Lauber also noted diminished excretion after operation and after experimental infection in rabbits. At the same time Geissendörfer[3] reported that a patient with a colloid goiter was prepared for operation by the administration of 100 mg. of cevitamic acid daily until the excretion became constant at 20 mg. per day. The day after the operation the output rose above 50 mg.; it fell gradually during the following week. Another patient with hyperthyroidism, treated in the same way, showed an excretion of less than 10 mg. daily before operation, and for five days after operation the excretion was exceedingly low but rose thereafter to more normal values. It should be borne in mind that the tissue demands for vitamin C are increased in hyperthyroidism. In 1938 Griebel[4] studied the problem of vitamin C balance by means of the administration of large doses of cevitamic acid. He found a negative balance after operation as well as in febrile diseases, indicating to him that in both cases there was an increased demand for the vitamin. As these results are seemingly contradictory no conclusions can be drawn except that anesthesia and operation, both in animals and in human beings, may either increase or decrease the urinary output of the vitamin.

TABLE 1. *Effect of Operation on Serum Ascorbic Acid.**

OPERATION	SERUM ASCORBIC ACID			
	PREOPERATIVELY			POSTOPERATIVELY
	Avg.	Max.	Min.	Avg.
	mg. per liter	*mg. per liter*	*mg. per liter*	*mg. per liter*
Appendectomy	5.85	9.40	3.29	4.70
Cholecystectomy ...	8.55	15.50	3.29	3.29

*Extract from Bazzocchi's "Table 2."

Bazzocchi[5] in 1936 studied the serum ascorbic acid levels in surgical patients before and after operation. He used a trichloracetic precipitation method for his determinations. The end point was determined by the amount of decolorizing of methylene blue that took place on ten minutes' exposure to sunlight. It is possible that this is not a very accurate method, but the results were reasonable. Bazzocchi found serum values rang-

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ing from 1.55 to 0.14 mg. per 100 cc. in miscellaneous surgical patients; the average value was 0.56 mg. He stated that after operation the values tended to diminish. The data on which this statement was based are not presented in tables of individual cases, but only as shown in Table 1. Unfortunately this table, like all other information in Bazzocchi's paper, indicates neither the number of cases studied, the number of determinations per case either before or after operation nor the length of time the studies were carried out before or after operation.

This report contains much more information concerning the effect of operation on the urinary ascorbic acid values than do other papers. Unfortunately it is presented in the same obscure fashion as are the serum data. However, Bazzocchi made the following conclusions:

> In surgical patients the amount of vitamin C excreted in the urine varies within rather wide limits. It is less than normal, for example, in gastroduodenal ulcer and in adhesive syndromes of the right abdomen, but higher than normal in intestinal occlusions and in surgical affections of the kidney. In Basedow's disease the amount excreted is high, but falls below normal after thyroidectomy.
>
> In the postoperative period, the values tend to approach normal. After cholecystectomy there is a sudden diminution of elimination.
>
> If determinations are carried out immediately before and after intervention, taking into account the different types of anesthesia, a diminution is as a rule observed after ether narcosis and after peridural and local anesthesia, but an increase after evipan anesthesia.
>
> Ascorbic acid is present in the serum of surgical patients in the proportion of 5.60 mg. per liter on an average. As a rule the amounts found have been smaller than those in the urine.

METHODS

No studies were made by us on the urine. It has been shown by many authors that appreciable urinary secretion of the acid takes place only when excess amounts are fed to a saturated patient and that many patients are not saturated. Blood specimens were taken in the early morning and determinations on the plasma were made by a modification of the Farmer and Abt[6] method. The details of our technic and possible explanations of our rather low average figures will be considered in another paper. Whenever possible two or more determinations were made before operation and several after operation. In order to keep the study free from the complicating factor of the effect of high fever on the metabolism of the acid, all cases that developed pneumonia or other infections were eliminated from the series. None of the patients tabulated were given cevitamic acid treatments before the last determination.

RESULTS

The cases studied have been divided into four groups according to the preoperative level of the plasma cevitamic acid. The first group consists of cases in which the levels may be considered to be normal (at least 0.8 mg. per 100 cc. of plasma). In the second group the levels are generally considered to be low normal (0.5 to 0.8 mg. per 100 cc.); these levels are below those of fully saturated patients, but no harm is known to result from the maintenance of such levels. The third group is made up of patients with levels (0.2 to 0.5 mg. per 100 cc.) which are supposed to result in symptoms of chronic scurvy if maintained. In the fourth group the levels were less than 0.2 mg. per 100 cc.; if the blood remains below this level for a few weeks some or all such patients develop active scurvy.

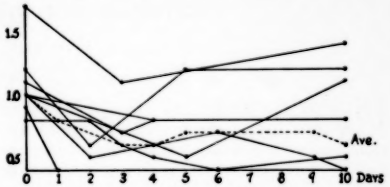

CHART 1. *Effect of Operation on Blood Plasma Cevitamic Acid Level.*

Nine cases with initial levels at 0.8 mg. per 100 cc. or higher.

In the tables the bold-face figures are actual determinations, while the others are interpolations. These interpolations are inserted for one reason only, namely to allow the calculation of relatively significant averages. It was manifestly impossible to take daily blood specimens, and yet without daily figures the averages resulting from each day's figures would jump about so much as to be valueless.

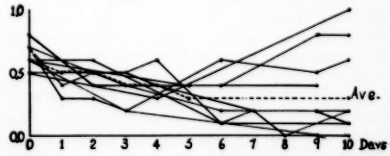

CHART 2. *Effect of Operation on Blood Plasma Cevitamic Acid Level.*

Ten cases with initial levels between 0.5 and 0.8 mg. per 100 cc.

Chart 1 and Table 2 show that in patients with normal preoperative levels the vitamin level was reduced postoperatively about 30 per cent on the average and not over 50 per cent in any individual case within three days after operation, and that only occasionally was there a tendency for it to return to its former level during the follow-up period. In none of these cases were any postoperative values of less than 0.4 mg. per 100 cc. found.

Chart 2 and Table 3 give the data on the cases that showed suboptimal but not extremely low values at the start. These cases on the average dropped 50 per cent, and several patients showed a loss of nearly all the vitamin from the blood. Only 3 cases showed any tendency for the level to rise after it had gone down. These data show that when the preoperative blood level is originally only slightly above those which might have resulted in scurvy if maintained long enough. The very low original level either persisted or dropped still further. However, in 4 cases there was a late rise to a level equal to or higher than the original.

Chart 4 and Table 5 show the results in the large group of cases in which the preoperative values were at the scurvy level. That means that these patients probably had very little tissue reserve which kept them from actual clinical scurvy. The original levels were so low that there could be no appreciable drop. In only 2 cases was there a late rise in the plasma level.

TABLE 2. *Effect of Operation on Blood Plasma Cevitamic Acid Level (9 Cases with Preoperative Levels of 0.8 mg. per 100 cc. or Over).*

Case No.	Operation	Month	Plasma Cevitamic Acid Levels										Anesthesia
			Preoperative	Postoperative (days)									
				1	2	3	4	5	6	7	8	9	10	
			mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	
1	Excision of sinus tract	May	1.7	1.5	1.3	1.1	1.1	1.2	1.2	1.3	1.3	1.4	1.4	Nitrous oxide and ether
2	Appendectomy	March	1.2	0.9	0.6	0.8	1.0	1.2	1.2	1.2	1.2	1.2	1.2	Spinal
3	Cholecystectomy	December	1.1	1.0	0.8	0.7	0.8	0.8	0.8	0.8	0.8	1.1	1.1	Nitrous oxide and ether
4	Exploratory laparotomy; normal pregnancy	March	1.0	0.8	0.5	0.6	0.6	0.7	0.7	0.6	0.5	0.5	0.4	Spinal
5	Cholecystectomy with drainage	May	1.0	0.9	0.8	0.7	0.6	0.5	0.5	0.5	0.5	0.6	0.6	Nitrous oxide and ether
6	Appendectomy excision; ovarian cyst (right)	December	1.0	0.8	0.7	0.6	0.5	0.5	0.4	0.5	0.5	0.5	0.5	Spinal, and nitrous oxide and ether
7	Appendectomy	March	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	Spinal
8	Cholecystectomy	April	0.9	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	Nitrous oxide and ether
9	Cholecystectomy	December	0.8	0.8	0.8	0.6	0.6	0.6	0.6	0.6	0.7	0.7	0.8	Nitrous oxide and ether
	Average		1.0	0.8	0.7	0.6	0.6	0.7	0.7	0.7	0.7	0.7	0.6	
	Maximum		1.7	1.5	1.3	1.1	1.1	1.2	1.2	1.3	1.3	1.4	1.4	
	Minimum		0.8	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	

TABLE 3. *Effect of Operation on Blood Plasma Cevitamic Acid Level (10 Cases with Preoperative Levels of 0.5 to 0.8 mg. per 100 cc.).*

Case No.	Operation	Month	Plasma Cevitamic Acid Levels										Anesthesia
			Preoperative	Postoperative (days)									
				1	2	3	4	5	6	7	8	9	10	
			mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	
1	Herniorrhaphy	April	0.8	0.6	0.4	0.4	0.4	0.4	0.4	0.5	0.6	0.8	0.8	Spinal
2	Appendectomy	December	0.7	0.4	0.5	0.5	0.6	0.4	0.1	0.2	0.2	0.2	0.1	Spinal
3	Cholecystectomy	April	0.7	0.6	0.5	0.4	0.3	0.3	0.2	0.2	0.2	0.2	0.2	Spinal
4	Cholecystectomy; choledochostomy	January	0.7	0.3	0.3	0.2	0.4	0.5	0.6	0.6	0.6	0.5	0.6	Nitrous oxide and ether
5	Exploratory biopsy; duodenal ulcer	April	0.6	0.5	0.3	0.2	0.1	0.1	0.1	0.1	0.0	0.0	0.0	Nitrous oxide and ether
6	Lysis of adhesions; resection of posterior jejunum	January	0.6	0.6	0.6	0.5	0.4	0.2	0.1	0.1	0.1	0.1	0.1	Nitrous oxide and ether
7	Cholecystectomy	December	0.6	0.6	0.7	0.3	0.4	0.3	0.3	0.2	0.0	0.1	0.2	Nitrous oxide and ether
8	Appendectomy	March	0.6	0.5	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4		Spinal
9	Herniorrhaphy	May	0.5	0.5	0.4	0.4	0.3	0.4	0.5	0.7	0.8	0.9	1.0	Spinal
10	Appendectomy	March	0.5	0.5	0.5	0.5	0.4	0.3	0.2	0.2	0.2	0.2	0.2	Nitrous oxide and ether
	Average		0.6	0.5	0.5	0.4	0.4	0.3	0.3	0.3	0.3	0.3	0.4	
	Maximum		0.8	0.6	0.7	0.5	0.6	0.5	0.6	0.7	0.8	0.9	1.0	
	Minimum		0.5	0.3	0.2	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	

DISCUSSION

It is seen from the tables that when the plasma cevitamic acid level is above minimal values a somewhat low the drop following operation is on the average greater on a percentage basis than it is when the original level is normal.

Chart 3 and Table 4 give the data on cases where the preoperative level would not be considered in any way to be a low normal. These levels were drop occurs postoperatively. This drop is of the order of magnitude of from 30 to 50 per cent.

Changes in the plasma cevitamic acid level are influenced by changes in the intake, absorption or utilization of the vitamin. As mentioned above, none of these patients were given cevitamic acid,

therefore the only source was in the food. For one to three days after operation very little food was taken, or if food was taken, little of it retained. It was impossible for us to keep track of and consider the feeding of these patients as individuals. Their diet was the usual one given after such operations in this hospital.

CHART 3. *Effect of Operation on Blood Plasma Cevitamic Acid Level.*

Eleven cases with initial levels between 0.2 and 0.5 mg. per 100 cc.

CHART 4. *Effect of Operation on Blood Plasma Cevitamic Acid Level.*

Thirteen cases with initial levels less than 0.2 mg. per 100 cc.

However, it is well known that any infection or other cause of increased metabolism causes extra demands for this vitamin, and causes the plasma vitamin C level to fall if the vitamin is not supplied. After any operation, and without there being any definite complication, there is apt to be a slight fever for from two to four days. It is reasonable to suppose that extra amounts of this vitamin are used up because of the fever and its associated increase in metabolism. It is also possible that the demand of the newly formed tissues that are taking part in the healing process may use

TABLE 4. *Effect of Operation on Blood Plasma Cevitamic Acid Level (11 Cases with Preoperative Levels of 0.2 to 0.5 mg. per 100 cc.).*

Case No.	Operation	Month	Plasma Cevitamic Acid Levels											Anesthesia
			Preoperative	Postoperative (days)										
				1	2	3	4	5	6	7	8	9	10	
			mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	
1	Cholecystectomy	September	**0.4**	0.3	0.2	**0.0**	0.0	0.1	0.1	0.2	0.2	0.3	**0.3**	Nitrous oxide and ether
2	Hysterectomy	December	**0.3**	**0.3**	**0.1**	0.1	0.1	0.0	**0.0**	0.1	0.1	**0.2**	0.1	Nitrous oxide and ether
3	Closure of colostomy	December	**0.3**	0.2	0.2	**0.1**	0.1	0.2	0.2	0.2	0.2	0.3	0.2	Nitrous oxide and ether
4	Hernia	March	**0.3**	0.3	0.2	**0.1**	0.2	0.2	0.2	0.3	**0.3**	0.3	0.3	Spinal
5	Hernia	January	**0.3**	0.2	**0.2**	0.1	0.1	**0.0**	0.0	0.1	0.1	0.1	0.1	Spinal
6	Hernia	January	**0.3**	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	Spinal
7	Cholecystectomy	March	**0.3**	**0.3**	0.3	0.3	0.3	**0.3**	0.3	0.3	0.3	0.3	0.3	Nitrous oxide and ether
8	Hernia	April	**0.2**	0.2	**0.1**	0.2	0.2	0.2	0.2	0.1	0.1	**0.0**	0.0	Spinal
9	Hernia	December	**0.2**	0.2	0.2	0.2	0.1	0.1	**0.1**	0.2	0.3	0.5	0.6	Spinal
10	Hernia	January	**0.2**	0.2	0.3	0.3	0.3	**0.4**	0.3	0.2	0.2	0.1	**0.0**	Spinal
11	Hernia	March	**0.2**	0.2	0.2	0.2	0.2	0.2	0.2	**0.2**	0.2	0.3	0.4	Spinal
	Average		0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	
	Maximum		0.4	0.3	0.3	0.3	0.3	0.4	0.3	0.3	0.3	0.5	0.6	
	Minimum		0.2	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	

TABLE 5. *Effect of Operation on Blood Plasma Cevitamic Acid Level (13 Cases with Preoperative Levels below 0.2 mg. per 100 cc.).*

Case No.	Operation	Month	Plasma Cevitamic Acid Levels												Anesthesia
			Preoperative*	Postoperative (days)											
				1	2	3	4	5	6	7	8	9	10	11	
			mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	mg.	
1	Cholecystectomy	March	**0.2**	0.2	0.2	0.2	0.2	**0.2**	0.2	0.2	0.2	**0.2**	**0.2**	0.2	Spinal
2	Exploratory laparotomy; carcinoma of gall bladder	April	**0.2**	0.2	0.2	0.2	0.2	0.2	0.2	**0.2**	0.1	0.1	0.1	0.1	Spinal
3	Appendectomy	December	**0.2**	**0.2**	**0.0**	0.1	0.2	**0.3**	**0.2**	0.3	0.2	**0.0**	**0.0**	0.3	Nitrous oxide and ether
4	Cholecystectomy; choledochostomy	January	**0.2**	**0.0**	**0.3**	0.2	**0.2**	0.3	**0.3**	0.3	0.2	0.2	**0.2**	0.1	Nitrous oxide and ether
5	Supracervical hysterectomy	April	**0.0**	0.0	0.0	0.0	0.0	**0.0**	0.0	0.0	**0.0**	0.0	0.0	0.0	Nitrous oxide and ether
6	Colostomy	April	**0.0**	0.0	0.0	0.0	**0.0**	0.0	0.0	**0.0**	0.0	0.0	0.0	0.0	Nitrous oxide and ether
7	Herniorrhaphy	April	**0.0**	0.0	0.1	0.1	0.1	**0.1**	0.2	0.3	0.4	0.4	0.5	0.5	Spinal
8	Hernia	March	**0.0**	0.0	0.0	0.0	**0.0**	0.0	0.0	0.0	**0.0**	0.0	0.0	0.0	Spinal
9	Herniorrhaphy	March	**0.0**	0.0	0.0	0.1	0.1	0.1	0.1	**0.2**	0.2	**0.2**	0.2	0.2	Spinal
10	Hernia	April	**0.0**	0.0	0.0	**0.0**	0.0	0.0	**0.0**	0.1	0.1	0.2	**0.2**		Spinal
11	Cholecystectomy; exploration of common duct	September	**0.2**	0.2	0.1	**0.1**	0.1	0.1	0.2	0.2	0.2	0.2	**0.2**		Ether
12	Cholecystectomy; appendectomy	May	**0.0**	0.0	0.0	0.0	**0.0**	0.0	0.0	0.0	**0.0**	**0.0**	0.0	0.0	Nitrous oxide and ether
13	Cholecystectomy	July	**0.2**	0.1	**0.0**	0.0	0.0	0.0	**0.0**	0.0	0.0	0.0	0.0	0.0	Ether
	Average		0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	
	Maximum		0.2	0.2	0.3	0.2	0.2	0.3	0.3	0.3	0.4	0.4	0.5	0.5	
	Minimum		0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	

*All the values listed as "0.2 mg." ranged from 0.15 to 0.20 mg. per 100 cc. but are so listed because the second figure is not considered to be significant.

Without studying each point separately one cannot determine the relative importance of the different factors that might cause this drop. How-

up the vitamin at a rate faster than that for normal growth.

SUMMARY AND CONCLUSIONS

Plasma cevitamic acid determinations were made before and after operation on 43 patients coming to major operation.

In nearly every case there was a prompt fall after operation from the original level.

In a few cases the level began to rise again after four or five days.

Whether this fall is important from the standpoint of healing or recovery will be the subject of future study.

A low plasma vitamin C value in a blood drawn from a patient in the period immediately after operation may not be so significant an indication of depleted reserves as is a low value before operation.

I am indebted to Leo Kahn, Catherine Guenther, Katherine Washburn and Percy Lusona for their technical assistance.

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VERMONT STATE MEDICAL SOCIETY

PATHOLOGIC CONDITIONS IN THE BILIARY TRACT*

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MONTREAL

BEFORE proceeding with a consideration of the pathologic lesions of the biliary tract, I shall review briefly the histological anatomy of the gall bladder and the bile ducts.

The normal gall bladder consists of five coats. From within outward they are the tunica mucosa, tunica muscularis, tunica fibrosa, tunica subserosa and tunica serosa. The last two are part of the general peritoneal structure and do not properly belong to the gall bladder. They consist of the peritoneum and subperitoneal tissue where they cover the gall bladder. The first three coats mentioned constitute the gall bladder proper.

The tunica mucosa consists of a lining of tall, columnar epithelial cells with rounded or oval nuclei situated near their bases. These cells secrete a mucus-like substance which on appropriate staining is seen as minute droplets at the free margins of the cells. Specks of bile pigment and minute quantities of lipoids are found near the base of the cells. According to Boyd[1] the normal mucosa of the gall bladder contains by dried weight about 0.6 per cent of lipoids. The epithelium rests on the delicate and loosely arranged connective tissue — lamina propria — of the mucosa. The surface area of the mucosa in the non-distended gall bladder is much larger than that of the other coats, and to accommodate itself to its enclosure it is thrown into folds which form, roughly, polygonal figures resembling the face of a waffle iron. On section they appear as papillae. The longer folds lie in the long axis of the gall bladder. There are no glands in the body of the normal gall bladder, but at its neck are found tubuloalveolar glands similar to those in the bile ducts.

The second coat, the tunica muscularis, is composed of bundles of smooth muscle separated by strands of loose connective tissue.

The third coat, the tunica fibrosa, is a fairly robust, complete fibroelastic investment which carries the larger vessels and nerves supplying the gall bladder. At the liver attachment of the gall bladder the tunica fibrosa is continuous with Glisson's capsule. In this area may be found ducts lined by columnar epithelium. They are present in the embryo as well as in the adult. They do not connect with the gall bladder but are continuations of bile ducts from the liver, and are known as Luschka's ducts.

The extrahepatic bile ducts are somewhat similar in structure to the gall bladder, but elastic tissue is much more plentiful and muscle is very scanty except at the sphincter of Oddi. Tubuloalveolar glands are numerous in their walls and extend deeply, even beyond the walls where they become invested with a fibroelastic coat.

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Absence of the gall bladder in human beings is rare, and only a single case is on record in our files. In this case the cystic duct as well as the gall bladder was absent. It is interesting to note that there was a stone impacted at the ampulla of Vater. The ducts were dilated and filled with pus. In another case the gall bladder lay under the left lobe of the liver. Before assuming the absence of the gall bladder, one should seek it embedded in the right lobe of the liver, or in an anomalous position under or behind the liver. Another unusual anomaly in our records is that of a greatly enlarged gall bladder, about the size of a baby's head. Otherwise it appeared normal. The bile ducts were normal, and bile could be expelled through the ampulla by slight pressure on the gall bladder.

A not uncommon variant in the structure of the gall bladder, which is of some interest pathologically, is that in which the fundus is partitioned from the body by a partial diaphragm. When the gall bladder is distended this diaphragm remains rigid causing a kink at this point. It is this condition that produces the Phrygian-cap effect referred to so frequently by radiologists. Stones may become impacted in the fundus behind this diaphragm.

Floating gall bladders are liable to torsion, with consequent infarction and gangrene.

The commonest and therefore the most important pathologic conditions are those related to stone formation, infection and tumor. These three, especially the first two, are so intimately associated and interdependent that it is difficult to consider them separately; hence, I shall follow in sequence the various phases of evolution of these pathologic conditions as encountered in the laboratory.

It is not my intention to enter into the controversy concerning the formation of gallstones. For this the reader is referred to the voluminous literature on the subject, but especially those papers by Aschoff,[2] Mackey,[3] Boyd[1] and Rufanov.[4] It is generally agreed that two factors enter into the formation of gallstones anywhere in the biliary tract, particularly in the liver and the gall bladder. The first of these is metabolic, for example the increase of cholesterol in the blood or excessive breakdown of red blood cells, as in hemolytic jaundice, and pathologic conditions of the liver which alter the content of bile acids. The second factor is stasis and infection. The extensive ramifications of the biliary tract in the liver, its small sphincter-controlled opening into the duodenum and the small neck and duct of the gall bladder are features which favor obstruction.

The commonest lesion in the gall bladder is cholesterolosis. This term indicates a condition in which there is an accumulation of lipoid material, mostly cholesterol esters, in the mucous membrane. It collects chiefly in the folds of the mucosa, and appears as yellowish flecks or streaks which stand out distinctly on the red or green background of the gall bladder, its appearance resembling that of a ripe or green strawberry. Because of this appearance McCarthy in 1910 coined the term "strawberry gall bladder," which has since been widely used.

The lipoids are contained within large cells in the lamina propria of the mucosa and as minute droplets in the bases of the epithelial cells, and appear in the usual paraffin sections as clusters of large, pale, foamy cells which distend the folds. Boyd[1] has shown that the mucosa of such a gall bladder may contain as much as 60 per cent by dried weight of lipoid, as against 0.6 per cent in the normal gall bladder. Variable amounts of lipoids have been found in from 37 to 50 per cent of all gall bladders examined at autopsy. The condition is believed to be due to an excess of cholesterin in the bile and the inability of the gall bladder to take care of its forced absorption.

Many authors in the past believed that this condition was a form of cholecystitis, since inflammation was often associated, and that it demanded cholecystectomy. Numerous other writers disagree, since in many cases no signs of inflammation can be detected; yet it indicates a condition which favors stone formation, and until some method is known whereby the condition can be corrected, cholecystectomy is indicated since it eliminates the possibility of cholelithiasis, with all its dire consequences.

Gallstones are found in the gall bladder in about one third of all cases of cholesterolosis. The stone is sometimes single, and may become very large. It is composed entirely of cholesterin which is precipitated from the bile. Aschoff[2] states that this is the only certain metabolic type of stone formed in the gall bladder, but considers other possibilities. However, another common type of stone associated with cholesterolosis is the smaller mulberry stone, which Mackey[3] believes is a cholesterin precipitation on a small nucleus of pigment calcium stones which form in the ducts of the liver and are passed on to the gall bladder. This type of stone is composed of a dark, soft center, with cholesterin crystals arranged radially about it and must be considered of metabolic type.

This common condition of cholesterolosis and mulberry stones, often present with slight or no symptoms, is extremely important. By their presence and by their possible impaction and interference with the drainage of the gall bladder

such stones probably form the most important etiologic factor in the more serious inflammatory conditions of this organ.

That infection may find its way to the gall bladder by way of the lymph vessels or blood stream, particularly the latter, is undoubted. Wilkie[5] has demonstrated this fact experimentally, and it is often supported clinically. For instance, a woman of thirty-seven gave a history of good health until she had a quinsy. Nine days later she developed acute upper abdominal pain and was quite ill. Five days later she was admitted to the Montreal General Hospital and was operated on. An acute gangrenous and hemorrhagic cholecystitis was found. Cholecystectomy was done, with recovery. There were no stones and no evidence of previous chronic cholecystitis, and the bile ducts were normal.

In the case of more attenuated infections, a chronic inflammation develops. The normal absorptive function of the gall bladder is interfered with and the inflammatory exudate, rich in calcium and protein, delivered into the lumen of the gall bladder gives rise to stones composed of cholesterin, pigment, calcium and inflammatory debris. These are usually multiple and may occur in enormous numbers. By their contact with each other they become angular and faceted. On section they are seen to be made up of cholesterin, pigment, calcium and inflammatory debris arranged in concentric laminae, or have a soft, dark-brown pigment-calcium center with a concentrically layered capsule of harder material containing cholesterin and calcium and may possess a thin coating of friable dark-brown or black material composed of pigment and calcium. These are the stones known as "infectious stones."

Once stones are formed in the gall bladder, the stage is set for a new train of events, that is, those following obstruction. Impaction in the neck of the gall bladder or the cystic duct favors infection from the infected static bile or by way of the blood stream. By far the majority of cases of acute cholecystitis are secondary to stone impaction rather than primary infections. In the case of obstruction by cholesterol stones and an attenuated infection with resulting chronic cholecystitis, there is added to the cholesterin stones already present the infectious type of stone. This may form a new coating for the old stones, and the latter may assume any of several forms. Additional stones of the infectious type form. We may then find one or a few larger stones or mulberry stones, with numerous infectious stones of fairly uniform size. If infection does not occur, or if it occurs and dies out, the epithelium continues to secrete mucus, filling or distending the gall bladder with "white bile" and forming a mucocele.

The changes seen in chronic cholecystitis vary markedly. Chronic inflammatory cell infiltration, atrophy of the mucosa and muscularis and productive fibrosis may go on to complete fibrosis of the wall with contraction and obliteration. This, however, is not usual. Instead, there may be productive fibrosis and great thickening of the tunica fibrosa. The muscularis hypertrophies and may even become hyperplastic, and epithelial hyperplasia may become quite active.

An almost constant finding is the development of epithelial crypts extending from the mucosa into and even through the muscularis between the muscle bundles. These are known as Rokitansky-Aschoff sinuses. Tubuloalveolar glands like those seen in the bile ducts may develop. In an exaggerated form this epithelial hyperplasia may assume the form of polypoid adenomatous structures, bulging into the lumen or lining almost the whole gall bladder, thickening the wall or protruding on the external surface. Usually the knobs are no larger than a marble, but great dimensions may be reached, as in a case reported by Wiglesworth,[6] of ten years' duration, in which the tumor attained the size of a large grapefruit. This condition is seen at the fundus more often than elsewhere. I believe that under the stimulus of chronic infections the gall bladder reverts to its embryonic form and begins to grow again, producing bile ducts with their glands, and abortive gall bladders in the form of cysts.

King and MacCallum[7] have named this condition cholecystitis glandularis proliferans (cystica). It is important that it be not mistaken for carcinoma. It is probable that many reported papillomas are really nodules of this process. Its relation to cancer is uncertain. King and MacCallum believe that cancer is no more liable to develop from this condition than from gall bladders without it, yet the very common association of carcinoma with chronic cholecystitis and the high incidence of cholecystitis glandularis proliferans suggest that there may be a close relation. A specimen of carcinoma of the gall bladder, from the Montreal Jewish General Hospital, which we had the privilege of examining recently appeared to have originated from this condition.

In our records the majority of perforations of the gall bladder or bile ducts occurred following acute cholecystitis secondary to impacted stones or to ulceration in the bed of a stone.

Perforation into the duodenum with the escape of stones is not uncommon. I have seen two such cases in which the escape of a large stone into the intestine resulted in fatal obstruction when

the stone reached the ileocecal valve. In two of our autopsy cases with stone in the common duct, perforation of the duct was followed by generalized bile and suppurative peritonitis. In one, the stone had ulcerated through the duct wall and lay in the periductal tissue. This stone could not be felt with the exploring probe. A biliary fistula followed the ulceration, with resulting peritonitis.

There are reported in the literature several cases of bile peritonitis due to seepage of bile from the gall bladder or ducts without any perforation. We have not observed any such condition. It is probable that in these cases a minute perforation had occurred somewhere. The two in the common duct just referred to might easily have been overlooked.

Congenital atresia of the bile ducts may be due to two conditions: failure of the ducts to canalize and fetal intrauterine infections. The second condition is believed to be commoner. In a month-old baby the common duct was markedly narrowed and no bile had entered the intestine. Histological section revealed an intact mucosa lined by epithelium. The lumen was not obliterated but was markedly constricted by chronic inflammation and fibrosis of the wall.

Tumors other than those of epithelial origin are rare, but submucous lipoma, fibroma and neuroma have been reported. Of the epithelial tumors there are the benign papilloma and the carcinoma.

In the gall bladder, papillomas, unless they bleed or cause obstruction at the neck, are usually accidental findings. In the ducts they cause obstruction and must be dealt with accordingly. They appear as papillary outgrowths from the mucosa, and although they may invade the wall they may still be benign. Carcinoma may develop at the base of a papilloma.

In one of our cases, a woman of sixty-four, there was a large papilloma in the body near the fundus, another near the neck and an obstructing one in the cystic duct. The gall bladder was dilated and filled with blood. There were no stones and no cholecystitis. In another case the tumor was in the common bile duct and was successfully removed.

That papilloma of the biliary tract is not infrequently multiple should always be kept in mind. It may be associated with papilloma of the duodenum at the ampulla of Vater, as was illustrated by a recent case of obstructive jaundice operated on at the Montreal General Hospital. A large papilloma was found in the duodenum at the ampulla, which at first was thought to be the cause of the obstruction, but as the surgeon prepared to remove it he discovered that the lower parts of the common bile duct and pancreatic duct were plugged with similar growths.

Carcinomas of the gall bladder and bile ducts are usually adenocarcinomas but may be of the simplex type. Their form may be villous, nodular or diffuse. When diffuse the gall bladder or ducts may be converted into a thickened, rigid tube. Mucous secretion by an adenocarcinoma may be a prominent feature, producing a gelatinous cancer. A favorite site of origin is near the neck of the gall bladder with obstruction and resulting dilatation and suppuration of the remainder of the body and fundus which may become palpable through the abdominal wall. Not infrequently the whole gall bladder is diffusely infiltrated, thickened and indurated.

The gall bladder may shrink to a small, hard mass, frequently encasing stones. On the other hand, very bulky gelatinous or villous tumors may greatly distend the gall bladder or form large masses adherent to and infiltrating the surrounding viscera. Small villous tumors in the fundus offer the best prognosis. A man of forty-two had had repeated attacks of biliary colic. The gall bladder was found greatly distended with blood and there were clots in the common duct. In the fundus was a small papillary carcinoma from which the bleeding originated.

Extension to the liver is common, as well as more distant metastases. An important secondary growth is that which occurs in the ovaries and which may reach bulky dimensions.

The association of carcinoma of the gall bladder with stones is exceedingly common. In our own material this association was seen in 70 per cent, and with chronic cholecystitis in 77 per cent. Kaufmann[8] quotes the figure as 86 per cent. So it appears that gallstones and chronic cholecystitis play an important etiologic role. One is reminded again of the active, benign epithelial hyperplasia referred to above under chronic cholecystitis glandularis proliferans. Carcinoma of the gall bladder is more frequently found in women than in men, which is also the case with gallstones.

In the extrahepatic biliary ducts there is a great tendency to sclerosis of the tumor. Early stricture often leads to death before metastases occur. However, many cases metastasize early and the growth may become widespread. Depending on the position of the tumor the results of obstruction vary. In supposedly benign fibrous stricture, careful histological examination will often prove it to be carcinomatous.

In two of our patients in whom there was progressive jaundice but with bile in the feces, followed later by complete biliary obstruction, the tumor had involved first one hepatic duct, causing

obstruction and jaundice but with a normal flow of bile from the other duct until it too became involved causing complete obstruction.

Carcinoma of the extrahepatic bile ducts is less common than gall-bladder carcinoma, the ratio being about 1:4. In a review of 9523 consecutive autopsies at the Montreal General Hospital, reported by McLaughlin,[9] in which there were 782 carcinomas, 24 were in the gall bladder and 7 in the ducts. It is commoner in men than in women, the ratio being 3:2. The favorite site is at the junction of the three large ducts.

There is not the same amazing association with gallstones as in carcinoma of the gall bladder, yet they are present in about one third of the cases, and are considered by many to be an important etiologic factor.

From facts and opinions it would seem that the treatment of cholelithiasis, with or without symptoms, is indicated if the incidences of cholecystitis and of bile-duct and especially gall-bladder carcinoma are to be reduced.

SUMMARY

The histology and pathology of the biliary tract are reviewed.

Anomalies other than the common variations of the part are presented.

Special consideration is given to cholelithiasis and cholecystitis with particular attention to the role of disturbed liver metabolism and cholesterolosis of the gall bladder in the etiology of cholelithiasis and cholecystitis.

The condition referred to as cholecystitis glandularis proliferans (cystica) is described, and its development and its relation to carcinoma discussed.

The pathology of the common epithelial tumors, papilloma and carcinoma, of the extrahepatic biliary tract, and their relation to cholelithiasis and cholecystitis are summarized.

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CLINICAL NOTE

SULFANILAMIDE DRUG FEVER: A SECOND ATTACK OF SUDDEN ONSET*

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DURING the past two years sulfanilamide has been found to be so efficacious in the treatment of various disorders that the danger of its indiscriminate use must be kept constantly in mind; various undesirable effects have been commented upon by many others,[1] and need not be discussed here; but the following case report may help to emphasize another reason for caution in choosing the drug.

CASE REPORT

An 18-year-old boy was admitted to the infirmary on February 18, 1937, complaining of severe sore throat; the pharynx was diffusely inflamed, and the temperature was 102°F. A throat culture showed large numbers of beta-hemolytic streptococci, and on the day following admission the patient was started on 20 gr. of sulfanilamide given five times daily. His condition rapidly improved, and on the 6th day the temperature was normal and a throat culture showed very few colonies of beta-hemolytic streptococci. On the 12th day the patient complained of general malaise and a diffuse morbilliform rash appeared over the entire body.

In January, 1939, the patient developed an acute urethritis and sulfanilamide was prescribed by a consultant. On January 27 four doses of sulfanilamide of 20 gr. each were taken. During the afternoon, shortly after the second dose, general malaise with headache developed and at 7 o'clock in the evening the patient was admitted to the infirmary with a temperature of 100.2°F., headache, malaise and chilliness, and moderate cyanosis of the lips. The sulfanilamide therapy was stopped and fluids were forced; the following day the temperature reached 104°F. and the feeling of general malaise and other symptoms persisted; late that afternoon a faint rash was noticed, and on the following morning there was a diffuse morbilliform rash over the entire body. The white-blood-cell count at admission was 17,000, and this fell on the following day to 9000. On the 4th day the temperature became normal, and all the symptoms disappeared; the rash gradually faded, and had almost cleared up by the 6th day.

The patient in question was treated with sulfanilamide in 1937 because of a severe beta-hemolytic streptococcal pharyngitis developing in the course of a small epidemic.[2] At this time knowledge concerning the administration and dosage of the drug was limited, and the patient received a somewhat larger dose of sulfanilamide over a longer period of time than would probably be given today; he subsequently developed a typical sulfanilamide drug fever.

In January, 1939, sulfanilamide was prescribed when the patient developed an acute urethritis; four doses of sulfanilamide of 20 gr. each were followed in a few hours by malaise, headache, chilliness and fever, and in thirty-six hours by a diffuse, morbilliform rash. The absence of upper respiratory tract symptoms and the initial leukocytosis supported our impression that the malaise and fever were not associated with a mild type of influenza, which was somewhat prevalent in the community at that time, and the quick development of the rash seemed to justify the opinion that the entire illness was sulfanilamide drug fever. The administration of sulfanilamide was stopped directly after the onset of symptoms.

It seems logical to assume that in this case the course of sulfanilamide given in 1937 with its subsequent drug fever sensitized the patient to sulfanilamide, and that consequently only a relatively small amount of the drug was sufficient in 1939 to produce drug fever within a few hours after therapy had been started. In view of the possibility of sensitizing an individual to sulfanilamide by a course of treatment with the drug, still another reason for care in selecting it as a therapeutic agent is made evident. It would be unfortunate were one to find that a patient had previously been given sulfanilamide for a mild illness, or for one in which sulfanilamide is not effective, and was therefore unable to tolerate the drug when suffering from one of the very serious diseases in which it is so effective.

SUMMARY

A report is made of the rapid development of sulfanilamide drug fever after the administration of a small amount of sulfanilamide to a patient who two years previously had had sulfanilamide drug fever.

The possibility of sensitizing a patient to sulfanilamide is suggested as another factor in deciding as to whether the drug should be given.

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PAPERS FROM THE FAULKNER HOSPITAL

CONGENITAL ARTERIOVENOUS FISTULA

With A Report of a Case Relieved by Operation

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CONGENITAL arteriovenous fistula is a term applied to those anomalous communications between arteries and veins, without an intervening capillary circulation. Much confusion has existed concerning the nomenclature of this condition, it usually being described according to its superficial characteristics rather than on the basis of the underlying pathologic lesion. For example, some of the synonyms are: cavernous hemangioma, cirsoid aneurysm, arteriovenous aneurysm, hemihypertrophy of the extremities, and racemose arterial angioma. The fundamental process is the same whether in an extremity or the brain.

PHYSIOLOGY AND LOCAL EFFECTS

With increase of venous pressure as the result of direct arterial inflow, the veins take on certain characteristics of the arteries; that is, they enlarge, may pulsate, and contain calcium deposits, and the oxygen content of the blood approaches that of the arteries. The surface temperature of the involved part increases as the result of increased collateral circulation. Soft-tissue changes, in the nature of edema, thickening, atrophy and trophic disturbances, ensue as the result of circulatory deficiency. The healing powers of the skin are greatly diminished. In the bones lengthening usually occurs, provided the fistulas are present before the epiphyses fuse to the shaft. Rarely, as in one of the present cases, actual shortening and bone atrophy occur as the result of diminution in the amount of blood to the part. Thrills and bruits are occasionally detected, but since these signs reflect large fistulous communications, they are more frequently manifestations of acquired arteriovenous fistulas.

Systemically, a rise in the systolic and a lowering of the diastolic blood pressure, an increase in total blood volume, and enlargement of the heart may occur. The latter is more often seen in the acquired type. Occasionally, the bradycardiac reaction occurs. This phenomenon is brought about by closure of the fistula either by pressure or by operation, which results in a decrease in pulse rate, reversal changes in the diastolic and systolic pressures, and a lowering of venous pressure.

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DIAGNOSIS

The patient may not be aware of the underlying condition until trauma aggravates it. Occasionally, dyspnea and a rapid pulse, stigmas of cardiac hypertrophy secondary to a fistula, are the first symptoms to bring the patient to the doctor. As a rule, the appearance of distended veins, plus a feeling of increased warmth in the extremity, apprises the patient of his condition. The presence of varicosities, soft-tissue hypertrophy with accompanying trophic disturbances, increase in length of the limb, x-ray evidence of bone changes and, lastly but most important, the finding of arterial blood in the vein establishes the diagnosis. The bright-red color of arterial blood in a sample withdrawn from the vein into a syringe is an indication of increased oxygenization, but the most accurate method is the determination of the oxygen content of the blood by the Van Slyke[1] gasometric method, after it has been removed from the vein under oil.

TREATMENT

Operative treatment in this disease has been extremely unsatisfactory. The fistulas, as a rule, are small and multiple, and many of the communications are actually in bone. In a number of cases where the main vessels have been ligated in the course of operation, amputation of the limbs has been necessary. In a study of 27 cases, Lewis[2] reports 13 amputations — 6 of the upper and 7 of the lower extremity. In those cases where the fistulous communications are located in a small area of the limb, fractional ligation of the main trunks may well accomplish a successful result. Injection of the regional veins with sclerosing solutions offers help in certain cases where trophic disturbances, such as ulceration and eczema, occur. In 11 of the 13 cases in this report, the patients presented themselves with painful ulcerations of the feet and legs. All were healed after the adjacent veins had been obliterated and support of the legs carried out for a period of two or three

months. Injections may be repeated as often as necessary.

A complete cure is only rarely effected by operation. This results only if the following requirements in a given case are fulfilled: localization of the disease to one limb; absence of fistulas in bones; and a patient who is young and in such physical condition as to withstand a long and sometimes shock-producing operation. It was believed that the case reported below satisfied these conditions and, accordingly, an operation on the patient was performed.

REPORT OF CASE

H. M., a 23-year-old, single girl, was referred on March 7, 1938, by Dr. Arthur Jackson, of Everett, Massachusetts, for varicose veins of the right leg and thigh and a large hemangioma on the anterolateral aspect of the mid-thigh. These lesions had existed since birth. An operation for the removal of the varicosities and the angioma had been performed when the patient was 12 years of age, but recurrence followed within a short interval. For several years, the veins had increased rapidly in size and number. Soft-tissue swelling had produced easy fatigue, heaviness and warmth in the involved limb, and a tendency to excessive perspiration. During the year preceding admission, the patient had begun to tire easily and noted increasing dyspnea and palpitation of the heart on exertion. She no longer cared to engage in any exercise, such as dancing, and ordinary work was beginning to fatigue her. Bandages and other supports had not eased the heaviness of the leg. The patient was admitted to the Faulkner Hospital for study on June 15.

Physical examination revealed a well-developed girl in excellent condition except for the right thigh and leg. In relation to the history of probable cardiac distress, it may be stated that the heart sounds were normal and there was no cardiac hypertrophy. The right thigh and leg showed enormous varicosities spreading over their anterolateral and anteromesial aspects, apparently having their roots in a large angiomatous mass on the anterior mid-thigh, where there were numerous scars of previous incisions (Fig. 1). Soft-tissue swelling was tremendous, the right leg, with the patient in the recumbent position, measuring 37.5 cm. in circumference at the calf, as against 33.8 cm. at a corresponding point on the left leg, and 53.8 cm. in the right mid-thigh, as against 47.5 cm. in the left. There were no thrills, bruits or pulsations in the veins.

X-ray films of the long bones of both legs revealed no lengthening and no thickening of the femur or tibia on either side. There was no roentgenological evidence of cardiac enlargement. The electrocardiogram was negative. Skin-temperature determinations, using the Tycos Dermatherm, showed an increase at right mid-thigh, mid-leg and foot of approximately 2.5°F. over the corresponding points on the left extremity. The oxygen content of the venous blood from the right thigh was 19.3 vol. per cent, from the right leg, 18.7 vol. per cent, and from the unaffected opposite limb, 11 vol. per cent (a normal figure).

FIGURE 1. *Anterior and Lateral Views before Operation.*
Note the large distended veins and the angiomatous mass on the anterolateral aspect of the right thigh.

The patient submitted to operation June 23. The operation was performed under spinal anesthesia. A 30-cm. incision was made from a point just over the femoral artery at the inguinal ligament down the mesial aspect of the thigh to the junction of the middle and lower thirds. The femoral artery and vein were found

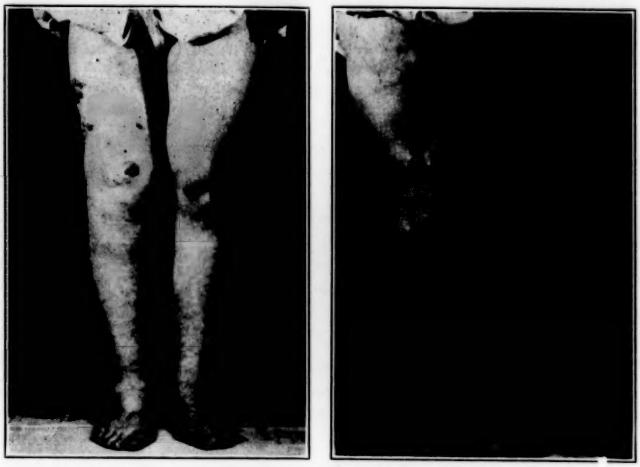

FIGURE 2. *Anterior and Lateral Views Six Months after Operation.*

and isolated without difficulty. The profunda femoris artery was also identified. The femoral vein was greatly distended and somewhat tortuous. Eight separate fistulas between the artery and vein were discovered in the exposed area. These were ligated with silk and divided. Some difficulty was experienced with one of these, where artery and vein were practically adherent for a distance of 1.0 cm. Further search revealed no more arteriovenous communications in this area. It was deemed inadvisable to explore the popliteal space. Several masses of varicosities were removed from the surface of the thigh. Considerable bleeding occurred from these areas, which proved to be venous tufts of the angiomatous mass. The patient stood the long operation well and was returned to her room in good condition. Her convalescence was uneventful, and she was discharged home after 2 weeks.

During the next 8 months, the patient's condition gradually improved. The wounds healed by first intention. The remaining varices were sclerosed by injections of sodium morrhuate and Monolate. The soft-tissue swelling of the thigh and leg subsided considerably (Fig. 2). The angioma gradually disappeared. Subjectively, the patient's fatigue and lassitude have gone and she no longer has dyspnea or palpitation. She is back at work and carrying on her active duties. No further operative procedure is contemplated.

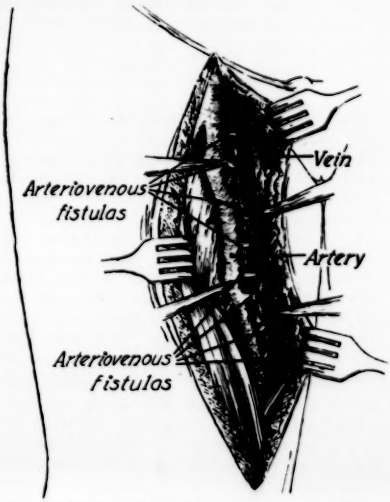

FIGURE 3. *Drawing of Operative Field Showing Arteriovenous Communications.*

Note the large fistula near the center of the incision, where the artery and vein are adherent for about 1 cm.

COMMENT

Congenital arteriovenous fistulas are still sufficiently rare to warrant reporting all cases. In a series of 447 cases of arteriovenous aneurysms collected by Callander and noted by McNealy,[3] only 3 were congenital. Lewis[2] reported 30 cases of congenital arteriovenous fistula in 1930, including 6 of his own. Horton,[1] in 1931, from the Mayo Clinic, reported 24 cases of congenital arteriovenous fistula, including those found in the extremities.

This present report is based on a series of cases observed by the writer over the past five years.

In the 13 cases listed in Table 1, there are several which require further comment. In Case 1, there was found an actual shortening of the involved limb, the only case of its kind which has come to our attention. In this case also were found a bruit, a thrill and the bradycardiac reaction, all ous operation. The fistulas, in this instance, were in the foot. Following the ligation of the main arterial trunk, two toes became gangrenous and amputation was necessary.

It should be noted in the table that in all cases in which oxygen determinations were carried out

TABLE 1. *Findings in 13 Cases of Congenital Arteriovenous Fistula.*

Case No.	Sex	Age	Location	Blood Pressure		Bone Involvement	Trophic Changes	Cardiac Hypertrophy	Increase in Surface Temperature	Other Clinical Manifestations	Oxygen Content	
											Involved Extremity	Corresponding Normal Extremity
		yr.		mm. of Hg.					°F.		vol. %	vol. %
1	F	19	Left arm	Left arm Right arm	140/90 120/85	Shortening	0		5.0	Bruit, thrill, bradycardia	17.4	9.2
2	F	17	Left arm	Left arm Right arm	152/100 130/90	Lengthening	0		3.5	Bruit, thrill, bradycardia	17.2	9.4
3	M	20	Left hand	Left arm Right arm	124/80 120/80	0	Eczema	0	2.0	0	16.5	10.2
4	F	34	Left foot	Both legs	126/90	0	Eczema, ulceration	0	3.0	0	18.0	10.1
5	F	29	Right leg	Both legs	118/80	Lengthening	Ulceration	0	1.2	0	17.5	9.5
6	M	35	Left leg	Both legs	132/90	Lengthening	Ulceration		2.4	0	17.8	11.0
7	M	50	Left foot	Both legs	150/110	Lengthening	Ulceration	0	0.5	Previous operation	13.9	10.9
8	F	18	Left leg	Both legs	110/78	0	Ulceration	0	4.2	0	—	—
9	F	14	Right leg	Both legs	118/80	0	Ulceration	0	4.0	0	—	—
10	F	22	Right leg	Both legs	130/90	Lengthening	Ulceration		3.2	0	—	—
11	M	40	Left leg	Both legs	114/74	Lengthening	Eczema		3.4	0	—	—
12	F	30	Left leg	Not taken		0	Eczema	0	1.2	0	18.7	10.8
13	F	23	Right leg	Right leg Left leg	140/100 122/66	0	Eczema	0	2.5	0	19.3	11.0

signs of large fistulous communications. In only one other patient, Case 3, did these phenomena occur. Bone lengthening occurred in 6 cases, and there were no bone changes in a like number. The most consistent findings in patients with congenital arteriovenous fistulas are trophic disturbances in the soft tissues. These occurred in 11 cases. The long duration and extensive involvement of the condition, with a background of deficient circulation, predispose to these changes. Atrophy of muscle and skin, with impaired vitality and susceptibility to minor infections, is characteristic. Ulceration, eczema, edema and fibrosis are later complications. Only one patient, Case 7, had had previ- there was a rise of oxygen in the venous blood which approximated that of arterial blood.

SUMMARY

Thirteen cases of congenital arteriovenous fistula are reported, with a detailed account of one, relieved by operation.

270 Commonwealth Avenue.

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THE MERIDEN HOSPITAL
MERIDEN, CONN.

CASE RECORDS OF THE FAULKNER HOSPITAL

Antemortem and Postmortem Records as Used in Monthly Clinicopathological Conferences

Directed by J. Beach Hazard, M.D.

CASE 6392

Presentation of Case

A thirty-two-year-old American waitress was admitted with the complaint of headache.

Eight months preceding admission she began to lose her capacity to concentrate and became quite irritable. Her vision had always been poor but at this time became worse. She also developed constipation whereas previously bowel habits had been normal. Five months preceding entry she began to have severe bilateral frontotemporal headaches which came on chiefly in the morning and afternoon. At times she was nauseated and vomited, the latter being on occasions of projectile type. She developed at about this time an unusual thirst which was accompanied by polyuria and nocturia of two times. Three months preceding entry she became so incapacitated that she had to discontinue her work. She visited her family physician who found that her blood pressure was 260 systolic. She was sent to a hospital for observation, and there she had skull and chest plates, both of which were said to be negative, as was a lumbar puncture. At about this time she had one attack of paralysis of the right arm which lasted a few hours. During a period of two weeks she menstruated twice, whereas previously catamenia had always been regular. Two and a half months before admission she entered another hospital where she had repeated lumbar punctures, which showed an initial pressure of 215 mm., dropping to 120 mm. after 10 cc. of fluid had been removed. There were no cells in the sample, the gold sol was 0000000000, the total protein was 75 mg. per 100 cc., and the sugar 67 mg. One intravenous renal function test at this time showed a phenolsulfonephthalein excretion of 5 per cent in fifteen minutes and 20 per cent in one hour, and a repeat test showed 15 per cent excretion in fifteen minutes and 40 per cent in one hour. An intravenous pyelogram revealed a normal-sized kidney with slight impairment of concentration of the dye. The total serum protein was 6.5 gm. per 100 cc., and the nonprotein nitrogen 28 mg. An eye consultant reported conical corneas in both eyes, with atrophy of the right optic nerve and choking of the left disk with some hemorrhage. Her blood pressure at this time was 245 systolic, 145 diastolic. Urine examinations showed a large trace of albumin, and all specimens contained many red cells. The specific gravity never went above 1.015. The average red-blood-cell count was 3,500,000 with a hemoglobin of 95 per cent (Tallqvist). Treatment consisted of intramuscular magnesium sulfate, venesection, lumbar puncture and sedatives, but did not give much relief. The headaches seemed to come in cycles and disappeared when her systolic blood-pressure level had decreased to about 200. She was discharged from the hospital about one month preceding admission. Following discharge she was at first well and then again began to have a severe headache, which was uncontrolled by huge doses of sedatives, venesection or the intravenous administration of 50 per cent glucose solution. After four or five days the headache was less severe, but she continued to vomit and to have attacks of aphonia, blindness and paralysis, all of which were transitory.

Her father had died at fifty-three of Bright's disease and carcinoma of the rectum. Several uncles and aunts had had Bright's disease. Her mother was sixty-one years old and living and well. Her husband was dead. She had had one pregnancy eight years before admission, which ended in a stillbirth. At this time her blood pressure was normal.

At the age of five she had received an injury to her right eye associated with a compound fracture of the skull and had been practically blind in that eye subsequently. She had had herpes zoster at ten years of age. A year before she was admitted to this hospital she had some teeth extracted and this was followed by a skin rash and arthritis which disappeared after a few weeks. She had been in good general health until her present illness.

Physical examination showed a well-developed and nourished, pale, restless woman, complaining of severe headache. There was an excess of hair on the legs and arms, and the pubic hair showed a masculine distribution. Her breasts were small. The eyes were exophthalmic, and the eyegrounds were not seen due to conical corneas. The pupils reacted to light. The throat and tongue were negative. The heart was enlarged 2 cm. to the left, but the right border was in a normal location; there was no increase in supracardiac dull-

ness. There was a soft systolic murmur at the apex. The pulse rate was regular. The lungs were clear. The abdomen was soft and presented slight tenderness in the epigastrium and in the lower abdomen on both sides. A vaginal examination revealed tenderness in the right vault, with pain on movement of the cervix. There were no masses, but the uterus was pulled over to the left and fixed. The knee jerks were normal, and there was no Babinski.

A catheterized specimen of urine was pinkish-brown, slightly alkaline and of a specific gravity of 1.014 and showed a heavy trace of albumin and no sugar; the sediment contained many red cells and numerous leukocytes. The white-cell count was 11,100 with 80 per cent polymorphonuclears. The red-cell count was 4,800,000 with a hemoglobin of 97 per cent (Sahli). The blood nonprotein nitrogen was 30 mg. per 100 cc., and the blood Hinton test was negative.

After admission, pain was relieved by ¼ gr. of morphine, but she was quite restless and vomited about 50 cc. of yellowish fluid. Breathing was at times irregular with a rate for a few hours of 15 but usually of 20. During the night of admission headache was controlled by ¼ gr. of morphine administered twice. A urine specimen on the second day of admission was reddish and slightly acid, with a specific gravity of 1.012, and contained a heavy trace of albumin but no sugar; the sediment was similar to that on the previous day. On the second day after entry she was quite talkative and seemed to be better oriented but complained of headache, chiefly on the right side. Breathing was at times irregular, and 7½ gr. of caffeine sodiobenzoate was administered. Several hours after eating a good dinner, she again developed severe pain in the right side of her head, for which ½ gr. of luminal was given, and shortly after this she became very restless and complained of pain in the neck; 7½ gr. of caffeine sodiobenzoate was given intramuscularly. About an hour later respirations seemed labored and caffeine sodiobenzoate was repeated. At this time her pulse was weak and irregular; the pulse rate was 100, and the respirations 8. Respirations ceased about half an hour later, but her heart kept on beating for ten minutes after breathing stopped. During her hospital stay her systolic blood pressure varied from 260 to 300, and her diastolic pressure rose constantly from 150 to 180. The temperature showed a gradual fall from 99.2 to 97.8°F.

Differential Diagnosis

Dr. Channing Frothingham: The medical internist has an advantage in these clinicopathological conferences because he knows he is considering a fatal disease whereas the surgeon may be presented with a problem solved just by biopsy.

This patient was admitted with the chief complaint of headache, and knowing it is a fatal disease we need not consider the conditions that have a favorable prognosis. Acute infection can be ruled out on the basis of the afebrile course. We are dealing with some type of chronic disease the outstanding symptom of which was headache. I think at once of the possibilities of nephritis and vascular disease, with the primary cause of the symptoms in her head. Added evidence of an intracranial lesion are the personality changes, the disturbance of vision and projectile vomiting. The development of constipation suggests the possibility of tumor even though her youth detracts from emphasizing a change of bowel habits. With symptoms suggesting an intracranial lesion a tumor metastatic from the intestine is to be considered.

The unusual thirst, polyuria and nocturia are suggestive of diabetes insipidus or diabetes mellitus. The latter can be readily ruled out. These symptoms are apt to occur also with disturbances in the circulation or a growth in or about the pituitary.

A systolic blood pressure of 260 is ordinarily too high to have been caused by a brain tumor. It is also higher than that usually associated with chronic vascular nephritis, and it makes me very suspicious that we are considering a patient who has a primary elevation of the blood pressure, the cause of which is probably unknown. The fleeting attack of paralysis of the right arm makes one think of a cerebral vascular accident, but the possibility of a brain tumor must still be kept in mind. The lumbar punctures done before admission only showed increased intracranial and spinal-fluid pressures, a finding which is consistent with tumor or goes with hypertension. The choking of the disk and retinal hemorrhage fit with vascular disease, intracranial new growth or chronic nephritis. Albumin and blood were present in the urine, but no mention is made of casts. This is unusual in chronic vascular nephritis, but in the type associated with destruction of afferent arterioles it is possible. The injury to her eye at the age of five years is of practically no importance in explaining her present symptoms.

The excess of hair on the legs and arms and the masculine distribution of pubic hair may be of some importance as certain types of hypertension are associated with lesions of the pituitary or adrenal glands. The soft systolic apical murmur does not necessarily mean valvular disease as it can be explained on the basis of hypertension. Tenderness in the right vault with pain on movement of the cervix might suggest some inflammatory le-

sion, but I cannot believe that is a factor. Deviation of the uterus to one side suggests new growth in view of the possibility of metastatic intracranial tumor.

In summary, the problem presented is that of a person who has hypertension accompanied by repeated cerebral vascular accidents. This makes me believe that we are going out of our way when we try to make a diagnosis of tumor. There is not a sufficient degree of peculiarity of the skin and skin appendages in the absence of growth disturbance to make me think too seriously of adenoma of the pituitary or adenoma of the adrenal. They generally present a different picture than this. Therefore, I am going to say that this patient has hypertensive vascular disease. If one accepts this conclusion, it must be decided whether it is the gradually progressive or the so-called malignant type. There is a difference in that the former usually shows lesions in the intima and a gradual thickening of the blood vessels, while in the latter, there is in addition an acute destructive lesion involving all the coats of the small arteries. If it is the malignant type of hypertensive vascular disease it may be more in evidence in the brain, in the heart or in the kidneys. I am going to say that, in this particular patient, it was the malignant type and that the lesions were more pronounced in the brain and in the kidneys than they were in the heart; the reason I say so is because there are very few symptoms pointing toward the latter, except hypertrophy. The several attacks consistent with vascular accident certainly point toward the brain, and the character of the urine, with much albumin and blood and nothing to suggest impairment of renal function or diffuse renal insufficiency, makes me think that there will be a lesion in the kidneys but it will be most evident in the afferent vessels to the glomeruli, the lesion which is supposed to be characteristic of malignant hypertensive vascular disease. As for the hypertension occurring with pituitary adenoma or adrenal tumor, I do not believe we have enough evidence to justify such a diagnosis, and it seems to me that the blood pressure is a little too high.

A Physician: Do you think there is any significance in the fact that her heart continued to beat for ten minutes after the respirations had ceased?

Dr. Frothingham: That does not mean anything to me. She apparently died from intracranial pressure. I think we shall find a fairly good-sized intracranial hemorrhage.

Dr. Edward L. Young: Is it too late to consider a traumatic cyst?

Dr. Frothingham: I do not believe that the symptoms of a cyst would be different from those of a gradually growing brain tumor, and with the latter there would be no reason for the condition in the kidneys.

Dr. David Halbersleben: Isn't a nonprotein nitrogen of 30 mg. per 100 cc. low for any important vascular disease of the kidneys?

Dr. Frothingham: I am making a diagnosis of malignant hypertensive vascular disease and believe that most of the lesions in this case are going to be in the head; there is only going to be a reasonable number of lesions in the afferent vessels of the kidneys and they have not yet completely destroyed renal function. Frequently the renal lesion is most important.

Clinical Diagnoses

Malignant hypertension.
Malignant nephrosclerosis.

Dr. Frothingham's Diagnoses

Hypertensive vascular disease, malignant type.
Cerebral hemorrhage.

Anatomical Diagnoses

Malignant nephrosclerosis.
Cerebral edema with cerebellar conus.
Myocardial hypertrophy.
Necrotizing arteriolitis: pancreas, duodenum, spleen, adrenals, gall bladder and kidneys.
Old salpingo-oophoritis, left.
Ruptured corpus hemorrhagicum, left.

Pathological Discussion

Dr. J. Beach Hazard: Dr. Frothingham's diagnosis of the underlying pathologic process is correct. The lesions present in this case were those that are found in the so-called malignant hypertensive disease. The kidneys were typical of malignant nephrosclerosis although the tubules did not show the marked dilatation that one sees in completely decompensated kidneys. This correlates with the findings of a normal nonprotein nitrogen. We expected to find a cerebral hemorrhage, but there was none. The brain was enlarged and there was marked cerebral edema and a cerebellar conus. The clinical picture is explained on the basis of this enlarged, wet brain. So-called hypertensive encephalopathy has two types of change as viewed at the autopsy table. One is marked cerebral edema with an associated cerebellar conus. The other is an anemia of the brain and suggests the possibility of vasospasm.

There was no tumor of the adrenal cortex or of the pituitary, though these possibilities are suggested by the change in secondary sexual characteristics. Necrotizing lesions were present in the arterioles of the small intestine, pancreas, spleen,

gall bladder, adrenals and kidneys, but there was practically no anatomic change in the vessels of the brain.

DR. JAMES A. HALSTED: In regard to treatment, the only thing to do was to try to relieve her headaches, and as the record states, she was given sedatives and glucose and had venesections. In one period of twenty-four hours she was given 9 gr. of Nembutal, ¾ gr. of morphine and venesection, none of which did any good in relieving the headache.

I should like to bring up the question of whether morphine in the presence of cerebral edema has an ill effect. I have an idea that, with cerebral edema, morphine is not a very good thing to give.

DR. HAZARD: I think it is an interesting point because in traumatic cerebral edema it is certainly not advised.

A PHYSICIAN: Was there any lesion in the pelvis?

DR. HAZARD: There was an old salpingo-oophoritis on the left which possibly accounted for the fact that the uterus was tilted over to the side. Also a ruptured corpus hemorrhagicum was found.

CASE 6393

PRESENTATION OF CASE

A forty-two-year-old American fruit dealer was admitted with the complaints of pain in the left leg and inability to move it.

Two days before entry, the patient was suddenly seized with severe abdominal cramps and collapsed. Shortly afterward excruciating pain began in the left leg and he was unable to move it. The leg was said to have been cold. About one hour later the pain lessened but the right leg became painful and cold to the level of the hip. A physician was called and prescribed morphine. The marked pain in the right leg and inability to move it persisted throughout the night and the patient was unable to sleep. The left leg had improved and was somewhat warm down to the knee, but below this was cold. During the night he vomited once. For the two days preceding admission there was little change. His bowels did not move during this time. Attacks of hiccoughing had occurred twice.

For six months the patient had been getting treatments for hypertension. His systolic blood pressure had been about 170. He was said to have been fibrillating for six months. He had been taking two tablets of digitalis daily. He had had rheumatic fever in his youth and was said to have had cardiac involvement.

The temperature on admission was 100°F., the pulse 100, and the respirations 22. The blood pressure was 86 systolic, 64 diastolic. The patient was stuporous and his face showed evidence of pain. The pupils were equal but sluggish; the ocular movements were normal. The tongue was dry and coated. Heart sounds were irregular in force and rhythm but were of fair quality. There was a marked pulse deficit. The right side of the abdomen presented a faint cyanosis which could be blanched by pressure. There was some edema on the right side. Moderate muscle spasm to deep pressure was evident on the right. Both arms were normal, and the radial pulses were felt. There was a slight cyanotic tinge to the fingernails. The left foot and lower leg were cold. The toes were pale with a grayish-yellow tint. The pulses of the femoral and popliteal arteries were good, but none were palpable in the foot. The oscillometer showed an absence of all pulsations below the tibial tubercle. Above this level the mean pressure was about 120, with 5 oscillometric units of expansion. The knee jerk was normal, the skin sensations were not tested. The right leg lay with foot drop and in eversion, and active motion was absent. The knee jerk was absent. The entire leg and foot were cold, very pale and grayish-yellow. There was marked edema up to and including the hip. The middle of the right thigh measured 51.2 cm., the left 46.2 cm. No pulsations of the iliac or femoral arteries could be detected on the right side and the oscillometer showed no pulsations in the mid-thigh.

A catheterized specimen of urine was of specific gravity 1.028 and showed a heavy trace of albumin and no sugar; the sediment contained 2 to 3 erythrocytes and 20 to 30 leukocytes per high-power field and frequent coarse granular and occasional fine granular casts. The white-cell count was 6700 with 73 per cent polymorphonuclears. The red-cell count was 4,200,000 with a hemoglobin of 89 per cent (Sahli). A smear showed slight achromia but otherwise was negative.

The patient was given 0.5 gm. of Mecholin every three hours by mouth, and ¼ gr. of morphine sulfate every three or four hours. On the day following admission the right limb was warm to the knee, but below was extremely cold with a bluish mottling which included the knee. The left leg was much warmer with a gradually developing coldness to the foot. The color was somewhat better. The blood pressure was 110 systolic, 70 diastolic. His bowels had not moved, nor had he urinated voluntarily. An enema had produced no result. The abdomen presented hyperperistalsis and he had several attacks of hiccoughing and tenderness in the right side of the

abdomen and a little shifting dullness in the flanks. Vomiting frequently occurred and fluids were stopped on the second day and glucose in saline solution was given intravenously. One and a half grains of digitalis daily was administered.

An enema on the third day was followed by a spontaneous bowel movement expelling considerable feces and gas. A urine examination showed a specific gravity of 1.021, no sugar, a trace of albumin, and a sediment contained 2 to 10 erythrocytes and 2 to 10 leukocytes per high-power field. He was stuporous but could be aroused and answered questions. On this day his temperature rose to 101°F. The abdomen was soft, but there was tenderness in the right lower quadrant. A slight icteric tint to the sclerae and the skin appeared. The icteric index was 100. The nonprotein nitrogen was 72 mg. per 100 cc. Diarrhea followed the period of constipation in the early portion of his stay but was readily controlled by kaolin and milk of bismuth. The icteric index on the fourth day was 60.

During the first six days after admission the left leg continually improved and the right developed a definite demarkation just below the knee. On the sixth day after entry his right leg was amputated between the middle and lower thirds of the thigh. A stool examination on the day of operation showed no occult blood. Following operation he was delirious, respirations increased, and rales appeared at both bases. The icteric index on the third postoperative day was 10, and a blood nonprotein nitrogen was 45 mg. per 100 cc. On the sixth postoperative day he developed ptosis of the left eyelid and a right lower facial paralysis. He continued to fail steadily, and on the ninth postoperative day he showed signs of pulmonary edema, developed a weaker pulse and died.

Differential Diagnosis

Dr. E. Everett O'Neil: I suppose one could begin this discussion giving a number of possible causes of pain in the legs, but I think we may restrict ourselves to the following three on the basis of his first complaint. These are: a ruptured plantaris tendon, which causes very acute pain in the posterior aspect of the leg, later accompanied by swelling and frequently thrombosis; thrombophlebitis; and acute arterial embolism. The diagnosis of ruptured plantaris tendon can be ruled out because there is no evidence of injury in this case. In regard to thrombophlebitis and acute arterial embolism it is interesting to note that the differential diagnosis between these is often difficult. Within the past year I have seen at least two cases that presented the usual clinical picture of arterial embolism but were finally diagnosed as acute thrombophlebitis. The textbooks so often tell us that the presence of a swollen leg, distended veins and warmth, plus a dusky pallor, indicates an acute thrombophlebitis. In the early stages these signs do not always obtain, and one might easily mistake the condition for an acute arterial embolism. It is a common observation that when an embolus has lodged at the bifurcation of the aorta or followed down to the bifurcation of the iliac arteries that the patient has abdominal cramps. Ordinarily, coldness of the leg is not consistent with thrombophlebitis and is definitely in favor of an obstruction in the arterial tree. In the early stages of an acute arterial block it is unusual to see such a complete process as this patient seems to have shown. The improvement that occurred in the left leg suggests that even though there was a block high up, it had either moved downward or the collateral blood supply had compensated for it.

The constipation and the moderate muscle spasm suggest that there was some process in the abdomen. It would be easy to postulate some other condition accounting for this, but in view of the subsequent story it does seem that it might well have been due to the same thing that had caused the lesions in the legs.

The cold foot and lower leg on the left observed on physical examination definitely fixed obstruction on that side in the popliteal region. The oscillometric measurements simply corroborate what we can make out by careful examination, and I think that by running the back of one's hand along the leg it is very easy to decide where the main trunks have been obstructed. The examination of the right leg revealed a block higher than that on the left, probably within the abdomen, presumably at the junction of the external and internal iliac arteries. The difference in measurements of the thighs suggests that in addition to the arterial block there was some secondary venous thrombosis.

In regard to therapy, I subscribe to the administration of morphine sulfate, but I am not sure that 0.5 gm. of Mecholin given by mouth would be of very great value. On the basis of clinical observation in these cases it would seem that a powerful antispasmodic is probably of value and should be given intravenously. I have been using ½ gr. of papaverine hydrochloride. As an alternative I believe that fairly large doses of alcohol by mouth are preferable to Mecholin. With a questionable arterial embolism, if the condition of the patient permits, a general anesthetic or spinal anesthetic would probably be of considerably more

value than any of these antispasmodic drugs in relieving the arterial spasm. The latter, above everything else, is a factor in those cases of arterial occlusion which go on to develop propagating thrombi.

The change in the right limb on the day following admission suggests that, in spite of the occlusion at the bifurcation of the iliac arteries, collateral circulation, of which there is an abundance in the upper thigh, had begun to act and increase the temperature of the part.

The hyperperistalsis, tenderness and shifting dullness suggest obstruction, probably in the lower small bowel. If we are postulating an arterial embolus, it is reasonable to suggest that on the way down to the peripheral blood vessels one of these thrombi stopped at the superior mesenteric artery and thus accounted for the ileus. It is a little difficult for me to explain the shifting dullness. The record says "a little shifting dullness in the flanks." I shall have to take that for what it is worth and say that there must have been some shifting dullness, but I am sure it is of no significance. If any of you have seen an embolus of the posterior mesenteric artery you will recall that the whole segment served by that particular branch is entirely blanched out, absolutely the antithesis of the picture which you see in venous thrombosis. The diarrhea following the period of constipation is in keeping with the cessation of obstruction of the superior mesenteric artery.

In retrospect, we have a forty-two-year-old man who had a sudden pain in the left leg which gradually improved and was followed by a similar pain in the right leg and again a pain in the lower abdomen. It is my opinion that this man in the presence of fibrillation, the result of old rheumatic heart disease, had an embolus which temporarily obstructed the orifice of the superior mesenteric artery, went on down and caused a saddle embolus at the bifurcation of the aorta. Part of the embolus, in turn, slipped out of this area down into the left popliteal bifurcation, and another lodged in the bifurcation of the right common iliac artery causing the picture which has been described. The condition went on to gangrene of the part, with death due to terminal pulmonary edema and pneumonia.

DR. DAVID HALBERSLEBEN: Have you ever used spinal anesthesia as an antispasmodic?

DR. O'NEIL: I have not tried it.

DR. HALBERSLEBEN: If you had been the first doctor called to see this patient would you have operated at once or would you have waited to see if the spasm could be relieved?

DR. O'NEIL: I would definitely have considered embolectomy in this case if I had seen him first. The two alternative methods to operating are: the use of an antispasmodic drug, which might do away with the necessity of operation, and the use of the suction-pressure apparatus, which should be supplementary.

DR. HALBERSLEBEN: How about occlusion of the brachial artery? In those cases are you as anxious to operate at once?

DR. O'NEIL: In any acute arterial occlusion I prefer to operate and the sooner the better, although this applies equally well to any therapeutic procedure that is carried out. An operation performed six or seven hours after the initial lesion does little, if any, good. I think we ascribe success to the suction-pressure therapy which it probably does not deserve because a good many of these emboli disseminate themselves or break up with relaxation of the spasm due to alcohol or drugs. If there is a block of a main vessel I prefer to go ahead and do an embolectomy.

CLINICAL DIAGNOSES

Multiple emboli.
Rheumatic heart disease, inactive, with fibrillation.

DR. O'NEIL'S DIAGNOSES

Old rheumatic heart disease.
Emboli to bifurcations of left popliteal artery and of right common iliac artery.
Pulmonary edema.
Pneumonia.

ANATOMICAL DIAGNOSES

Old rheumatic endocarditis of mitral valve with stenosis.
Mural thrombus, left auricle.
Embolic occlusion of right common iliac artery and left popliteal artery.
Thrombosis of left popliteal vein and right external iliac vein and tributaries.
Marantic endocarditis, mitral valve.
Recent infarcts of lungs and infarction of right kidney.
Old infarct of spleen.
Chronic passive congestion: lungs, liver and spleen.
Surgical absence of right leg.

PATHOLOGICAL DISCUSSION

DR. J. BEACH HAZARD: I think Dr. O'Neil has described the main pathologic changes about as accurately as we found them at autopsy. The right common iliac and the left popliteal arteries were filled with clot. The intestines were negative, and there was no obstruction in the superior

mesenteric artery. The urinary findings presented a problem when the patient came into the hospital. The explanation of this was extensive infarction of the right kidney due to occlusion of large branches of the renal artery. Examination of the brain revealed no anatomic lesion. The heart was enlarged and the mitral valve of "fish-mouth" type. A large mural thrombus was present in the left auricle. The lungs showed multiple infarcts, though at autopsy no thrombi were found in the right auricle. The cause of the jaundice was not apparent.

DR. JAMES A. HALSTED: Could jaundice have been accounted for by the pulmonary emboli?

DR. HAZARD: Yes, but the jaundice had cleared up before death; the icteric index was 10 at the last finding.

DR. EDWARD L. YOUNG: At what icteric index does slight clinical icterus develop?

DR. HAZARD: The range of latent jaundice without clinical signs is 6 to 15, but I have on occasions seen higher values than these without detectable icterus.

DR. HALSTED: Were there any signs of cardiac failure?

DR. HAZARD: There was chronic passive congestion.

REPORT ON MEDICAL PROGRESS

KIDNEY DISEASE

REGINALD FITZ, M.D.*

BOSTON

IN THE spring of 1937 the Class of 1912 of the Harvard Medical School celebrated its twenty-fifth anniversary. Dr. Henry A. Christian[1] gave a clinical lecture in which he rediscussed the general subject of nephritis for the benefit of his former students, contrasting present-day views with those held a quarter of a century ago.

Certain aspects of the nephritis problem are as old as the hills. The classification of the disease, for instance, will probably remain substantially unchanged. We recognize various forms of acute and chronic nephritis; but, as Dr. Christian said, while possibly we now find it more fashionable to speak of chronic glomerular or chronic vascular nephritis than to speak of chronic parenchymatous or chronic interstitial nephritis, as we used to, the character of these diseases remains the same.

Dr. Christian's paper is particularly stimulating because it shows so well how slowly clinical knowledge advances, and what a lag there is apt to be between new physiological concepts of disease on the one hand and their clinical application on the other. As an example of this he quoted Starling's work. It was in 1896 that Starling described the relation of the osmotic pressure of proteins to the fluid exchange between blood vessels and tissue spaces, pointing out that if the albumin content of the plasma was decreased, osmotic pressure changed and the fluid exuded from the vessels faster than it was taken up by the veins. It was ten years before clinicians realized the importance of this physiological idea, and another ten years before they began to apply it to clinical work. In view of such clinical conservatism, it is surprising that anything new of importance should be turned up in connection with so old and well plowed a field as that of Bright's disease. Yet new ideas regarding nephritis do appear from time to time, and some of them may be of value in practical therapy.

By all odds the most impressive single advance recently made in our clinical concept of Bright's disease has been due to Goldblatt[2] and his coworkers. In 1932 they began an attempt to produce hypertension experimentally. The method which they employed was an ingenious one: they studied the effect in animals of renal ischemia brought about by clamping the main renal artery with various degrees of constriction. From their early experiments they concluded that such renal ischemia, at least in dogs, did produce a persistently elevated blood pressure, and they found that almost complete constriction of both main renal arteries eventually resulted in great elevation of blood pressure, which was finally complicated by severe disturbance of renal function and uremia. They carried forward these observations, confirmed them in other species of animals and saw them in turn confirmed by other workers, until today the "Goldblatt animal" is

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familiar to all who are engaged in the field of experimental medicine.

As these things go, in a surprisingly short time after Goldblatt's early papers were published clinicians began to recognize "Goldblatt human beings." In other words, isolated cases began to be described in which hypertension appeared to be done away with by the removal of a unilateral renal lesion which had produced renal ischemia; cases, for example, of unilateral atrophic kidney due to a congenital anomaly of the renal artery as a result of which there had developed a true one-sided renal ischemia. Individuals such as these with hypertension are worth looking for. If they can be recognized and properly treated, they may form a group in which hypertension can be cured by a simple, direct surgical approach.

Interest in the surgical treatment of hypertension by sympathectomy has developed in recent years. Possibly its interest now is more acute than ever before because of Goldblatt's work.

It has been shown in animals that sympathectomy does not modify the hypertension resulting from experimental renal ischemia. In man too, this appears to be true. At the Robert Dawson Evans Memorial we have had a patient with hypertension treated by sympathectomy in whom the operation had no effect on the blood-pressure level. Later a one-sided atrophic kidney was removed and the blood pressure promptly fell to normal. Thus it appears that if sympathectomy is to be considered, accurate diagnosis is essential. If one is dealing with a "Goldblatt man," nephrectomy rather than sympathectomy is indicated if any form of surgery is in contemplation.

The present status of sympathetic-nervous-system surgery in relation to hypertension is not altogether clear. Among other workers in the field, Smithwick[3] has quite well demonstrated that significant blood-pressure changes may follow extensive sympathetic denervation, and that a lowering of the blood-pressure level may result from such operative procedures without harm to any organ or tissues of the body, and with relief from the distressing symptoms which may result from high blood-pressure levels. This effect is more than temporary, for many patients with abnormal blood-pressure levels have been continuously benefited from two to six years after operation. The best results obtainable from this approach occur in young patients with varying degrees of hypertension but with minimal evidence of organic changes in the eyegrounds, heart or kidneys. Unfortunately, even in such cases the results of surgery are not uniform. In hypertensive patients with advanced organic vascular changes, material lowering of the blood-pressure level by sympathetic surgery is to be expected but rarely.

On the whole, the surgical attack on hypertension by this method must still be regarded as in the experimental stage. It will take more experience to determine the most effective method of denervating any portion of the vascular bed. Further observations on the late results of treatment will be necessary in order to determine the indications for and the true value of sympathetic surgery in hypertension. There appear, however, to be enough encouraging results in carefully selected cases to justify further exploration by this means.

Massie, Ethridge and O'Hare[4] have recently revivified interest in the thiocyanate therapy of vascular hypertension. In 1925 this drug was introduced by Nichols for the purpose of lowering blood pressure, and during the following decade there appeared many articles dealing with its therapeutic usefulness. Some authors reported favorable results, others believed that the drug was ineffectual, or that its toxic effects were so frequently encountered and so dangerous as to interfere seriously with its administration.

In 1936 Barker introduced a method for blood-cyanate determinations and cyanate clearance tests in patients who were in need of the drug. His studies brought out two important and closely related facts. First he showed that the various reactions to the drug in different individuals were due in large measure to variations in ability to clear the blood stream of cyanate. Secondly, he demonstrated that by using as a control the level of cyanate in the blood he could regulate the dose accurately, largely avoid toxicity and often obtain a significant lowering of blood pressure. He concluded that the optimal therapeutic level of blood cyanate ranged between 8 and 12 mg. per 100 cc. Provided that dosage was regulated in this manner he considered thiocyanate administration a safe and effective treatment for selected cases of hypertension.

Massie, Ethridge and O'Hare agree with Barker. They believe that thiocyanate constitutes a useful drug for the treatment of uncomplicated vascular hypertension in certain cases, provided the dosage is scientifically controlled by means of blood-cyanate determinations. In the 14 cases which are the basis for their report, the dosage of thiocyanate was always gauged by the blood-cyanate concentration, the optimal level apparently ranging between 5 and 7 mg. per 100 cc. The daily amount of sodium thiocyanate required to maintain this level varied in different patients. A lowering of blood pressure was obtained in every case; the average fall in blood pressure in each case ranged from 66 to 21 mm. systolic and from 33 to 8 mm. diastolic. Marked symptomatic relief, especially in headaches, nervousness and vertigo, was ob-

tained in 12 of the 14 patients. Toxic symptoms were not often encountered, and these consisted merely of occasional episodes of transient weakness or infrequent attacks of mild epigastric distress. On the whole, the results of these investigators appear to be promising.

Finally, it must be remembered that occasional cases of paroxysmal hypertension have been described as being due to a tumor of the adrenal medulla, the removal of which has brought about a dramatic cure.

Thus at the present moment the management of hypertension is of greater clinical importance than ever before. When faced with a patient, who has persistent hypertension, one must now make sure that there is no adrenal tumor or no unilateral renal lesion producing ischemia, and one may properly ask whether the patient is likely to be benefited by a sympathectomy or by the use of a drug such as thiocyanate. In addition, one must not forget the knowledge that is already established regarding the management of hypertension; he must bear in mind the importance of a well-regulated life, of common sense, of weight control, of digitalis, and of the fact that hypertension may for years be a benign, harmless condition which is best treated by being severely left alone.

Along with increasing interest in the treatment of hypertension there has developed an interesting change in viewpoint regarding the essential pathology of many cases of chronic Bright's disease with high blood pressure.

Weiss and Parker[5] have recently analyzed 100 selected cases of pyelonephritis encountered in the Mallory Institute of the Boston City Hospital. They emphasize the importance of pyelonephritis in relation to chronic nephritis; they point out that the clinical course of pyelonephritis is strikingly variable, the renal infection often healing in a short time, although it may persist for years, during which time activity may be continuous or recurrent. They say that pyelitis practically never exists unaccompanied by pyelonephritis; and more important still, they conclude that pyelonephritis is responsible for between 15 and 20 per cent of the cases of malignant hypertension.

Pyelonephritis, therefore, must now be regarded as a very significant disease, for it is one renal disease which can be treated effectively in its incipient stage. It is worth remembering that a simple attack of acute pyelitis may be the beginning of chronic pyelonephritis with hypertension. Treatment must be instituted early, and no longer should pyelitis be regarded as a simple minor infection not requiring particularly careful supervision. All cases should be treated actively in the acute stage, with the idea of preventing the future development of chronic pyelonephritic lesions. The adequate treatment of acute pyelitis may be regarded as an important preventive measure against the subsequent development of a very common and hopeless form of chronic Bright's disease.

In the *Journal* for December 8, 1938, appeared an editorial entitled "Transfusion of Incompatible Blood." This was written in response to a letter by Dr. William Dameshek, published in the same issue, in which he commented on the fact that blood typing preliminary to transfusion carries with it a definite sense of responsibility and can never be done too carefully. As is well known, the transfusion of incompatible blood in man may be immediately followed by chills, fever, nausea and vomiting, acute pains in the muscles, dyspnea and a feeling of constriction in the chest. Signs of hemolysis may develop within a few hours. These include hemoglobinemia, hemoglobinuria and jaundice. If a relatively small amount of blood is hemolyzed, hemoglobinuria and jaundice may not be evident. The patient may recover, with nothing more serious than the loss of the transfused erythrocytes and consequent hemoglobinuria for several days. In some cases, however, the sequelae are grave: the urinary excretion is diminished or ceases entirely, the products of nitrogen metabolism increase rapidly in the blood, vomiting continues and generalized edema sometimes appears, coma gradually supervenes and the patient dies with the usual signs of uremia.

A paper of De Gowin, Warner, and Randall[6] is of practical importance in connection with this matter. These workers studied renal insufficiency in dogs produced by transfusion of canine hemoglobin, and showed that, when the urine was acid, death resulted from renal insufficiency. Obstruction of the renal tubules by hemoglobin pigment sufficient to be the chief cause of the renal insufficiency was observed in most dogs under the experimental conditions outlined. A study of the kidneys of 9 human beings who died of renal insufficiency after hemolysis of transfused blood revealed an extensive precipitation of hemoglobin pigment in the tubules. They suggest that this might be prevented by alkalinizing the urine prior to transfusion. The practical importance of such a suggestion is very obvious with transfusions being done as commonly as they are at the present moment.

Garvin and Van Wezel[7] have drawn attention to a peculiar form of kidney disease with which most clinicians are not familiar — bilateral cortical necrosis. It is rare, fortunately, but very striking. In such cases both kidneys are affected: the necrotic cortex appears reddish-yellow and soft, and closely

resembles a fresh infarct. However, the involved area has the shape not of an infarct but of a portion of cortex, even to the point of involving the columns of Bertin.

The etiology of bilateral cortical necrosis has been the subject of much investigation. So far as can be determined, the condition affects previously normal kidneys, and in the majority of cases there has been the preceding complication of pregnancy, often associated with antepartum hemorrhage. The clinical picture is fairly characteristic: the onset is acute; the paramount symptom is anuria; of less diagnostic importance are headache, nausea and vomiting, epigastric pain and occasionally edema and convulsions. The urine, if any is passed, contains albumin and casts, and occasionally blood and pus. The blood pressure is likely to remain normal; there is retention of nitrogenous products in the blood; the condition is almost always fatal. A few cases with recovery have been reported. The customary treatment consists of the intravenous administration of dextrose and the forcing of fluids.

Garvin and Van Wezel have described 3 fatal cases which were encountered in the Cleveland City Hospital in the past four years. These are of particular interest because they were not associated with pregnancy and because in each case in addition to cortical necrosis of the kidney there was marked central necrosis of the liver.

In brief, cortical necrosis of the kidney appears to be a renal condition worth emphasizing. It represents an unusual complication of pregnancy, dramatic in onset and recognizable only if the disease is considered.

Albright,[8] at the Massachusetts General Hospital, has made interesting studies concerning renal stones and their formation. Most kidney stones are composed of cystine, uric acid, calcium phosphate or calcium oxalate. In general, in the prophylactic management of patients with renal calculi, fluids should be forced. Then, depending on the chemical composition of the stone, the urine should be kept either alkaline or acid. For example, Albright suggests that when cystine and uric acid stones occur the urine should be kept alkaline, while in the presence of phosphate stones an attempt should be made to render the urine acid with an acid-ash diet and ammonium chloride. On the other hand, with calcium oxalate stones neither acid nor alkali therapy is indicated. Finally, calcium phosphate stones may be due to hyperparathyroidism, and in such cases eradication of the underlying disease is the method of cure.

It is interesting to realize how much more is known concerning kidney stones and their formation than was known even a few years ago. Albright now says that when a patient asks whether his stone can be dissolved, the question must not be regarded too lightly. Perhaps the time is not far off when it will be entirely possible to dissolve renal stones in vivo as well as in vitro.

Finally, when nowadays one thinks of medical progress, the universal clinical use of sulfanilamide or its kin comes to mind. At the various symposiums which have been held during the past year and at which sulfapyridine has been discussed, someone familiar with the matter was almost certain to tell the audience that this drug may be precipitated in the ureters or pelves, and thereby may produce albuminuria or hematuria. It is not known what may be the end result of renal irritation induced in this manner; probably the effect is transitory and of no importance. But at least it is worth bearing in mind that sulfapyridine may have a toxic effect on the kidney, and that the urine along with the blood and the patient must be carefully watched while the drug is being administered.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25301

PRESENTATION OF CASE

A fifty-year-old housewife was admitted on the orthopedic service complaining of pain and stiffness in the joints of the hands and legs.

The patient had been fairly well until six years before admission when she began to have pain, swelling and stiffness of the joints of both hands. These symptoms increased slowly, and she began to complain of pain and stiffness in the joints of the hands, legs and feet. She apparently suffered temporary relapses and remissions until one year before entry when she grew progressively worse. Four months before admission she became unable to walk. She had led an invalid existence since that time. One year before entry she had congestion in one or both eyes, and then developed unequal pupils, which persisted. She entered the hospital for the relief of joint pain and for the correction of flexion deformities of both knees.

The patient stated that she had had a "tiny" murmur in her heart for many years and had suffered "rheumatism" following a pregnancy twenty years before admission. Following this she had noted some shortness of breath on exertion and had had high blood pressure.

The marital and family histories were not contributory. The patient had had no cough, palpitation, angina or sputum. Her appetite had always been rather poor, but she had suffered no weight loss.

Physical examination revealed a well-developed and nourished woman in no apparent acute distress. There was a prominent flexion deformity of 90 degrees in the right knee. The examination on admission was otherwise negative.

Examination of the blood showed a red-cell count of 5,100,000 with 95 per cent hemoglobin, and a white-cell count of 19,200 with 82 per cent polymorphonuclears, 5 per cent lymphocytes, 5 per cent monocytes, 6 per cent eosinophils and 1 per cent basophils. The urine showed an acid reaction with specific gravity of 1.011 and 2 white blood cells and 4 epithelial cells per high-power field in the sediment; there was no albumin or sugar. The blood Hinton test was negative. The blood sedimentation rate for fifteen minutes was 2 mm., thirty minutes 8 mm., forty-five minutes 14 mm., and sixty minutes 19 mm.

At 12:30 a. m. on the third hospital day the patient suddenly developed an attack of rapid palpitation with left chest pain, not relieved by nitroglycerin. She became ashen, perspired freely, and when first seen by a house officer, was sitting on the edge of the bed, moving around freely, slightly cyanotic, with cold and moist extremities. The apex rate was 180 beats per minute and regular. It was not affected by carotid-sinus pressure. An electrocardiogram showed a ventricular rate of 100, with a P-R interval of 0.20 second, normal rhythm, marked left-axis deviation and inversion and slight widening of QRS_2 and QRS_3.

On the morning of the sixth hospital day the patient suddenly had severe dyspnea and clenched her teeth. The eyes became fixed, and the patient became unconscious and cyanotic. The pulse was 130 and regular. The blood pressure was 100 systolic, 60 diastolic, during or just after the attack, which lasted thirty seconds. Examination of the heart revealed a loud systolic blow with gallop rhythm and an amphoric A_2. Following this episode the patient seemed fairly well and posterior splints were applied to the legs to correct the flexion deformity. On the fourteenth hospital day her splints were removed because of pain in the legs. Examination of the heart at that time revealed that it was enlarged. There was a loud systolic blow and gallop rhythm with an amphoric A_2. The blood pressure was 130 systolic, 80 diastolic. On the nineteenth day examination of the heart revealed a loud blowing systolic murmur which replaced the first sound, gallop rhythm, and a short apical, musical diastolic murmur, which replaced the second sound. She developed attacks of dyspnea, and medium coarse rales were heard over both bases to the angle of the scapulas. On the twenty-first day an electrocardiogram revealed a ventricular rate of 90 and an auricular rate of 90, with normal rhythm. The P-R interval was 0.20 second. There was slight inversion of T_1 and T_4. There was considerable left-axis deviation and a slightly wide S_2.

On the twenty-seventh hospital day the patient became anuric for twenty-four hours and displayed Cheyne-Stokes respirations. The blood pressure was 120 systolic, 90 diastolic. The rhythm was rapid and regular at 110 beats a minute. There was pallor, but no cyanosis. Examination of the abdomen revealed slight shifting dullness. The liver edge was not felt. The following day she became cyanotic, vomited, and voided once. The liver edge was palpated. She rapidly failed and died.

Differential Diagnosis

Dr. Edward F. Bland: We are presented here with a fifty-year-old housewife who entered the hospital with chronic arthritis of some six years' duration. Otherwise according to the admission note she seemed fairly well. After three alarming episodes in the hospital, the first involving the heart, the second the brain and the third the kidneys, she gradually failed, and died approximately four weeks after entry.

In regard to her arthritis, the cause of her hospitalization on the orthopedic service, it seems reasonably clear that one is dealing here with the rheumatoid type. This conclusion is supported by the duration of her disease and the joints involved, especially those of the hands; I presume the wrists were also affected, although it is not so stated. Furthermore, the development of flexion deformities is most unusual with arthritis of other than the rheumatoid type. Finally, concerning the eye changes, we know that in rheumatoid arthritis episcleritis is fairly common, and although iritis is somewhat less common, it does occur; so I assume that this patient had had iritis in the past, with some deformity of the pupils thereafter.

We are told that the physical examination on admission to the hospital was normal except for flexion deformities of the knees. One wonders about that statement for several reasons. First, in view of the duration and extent of her arthritis there must have been chronic changes in joints other than the knees. Furthermore, mention is made elsewhere of hypertension and a heart murmur in the past, and we find in the first electrocardiogram marked left-axis deviation. Axis deviation of this order does not ordinarily occur in a short period of time but is the result of longstanding strain on the left ventricle, usually from hypertension or aortic valve disease. It is possible that this patient may have had a considerably elevated blood pressure in the past which may have slowly declined with her enforced inactivity in recent years. I wonder if there is a note giving the admission blood pressure.

Dr. Tracy B. Mallory: I cannot find it.

Dr. Bland: We come next to the first and only account of a blood examination, which is almost normal except for a leukocytosis of 19,000; this disturbs me somewhat. It is a little too high for uncomplicated rheumatoid arthritis. Since nothing further is said about it and the patient appeared otherwise well at the time of admission, I am forced with some reservation to discard this finding for the moment.

There is another finding here which lends some support to my belief that we had better not rely too much on this single white count: the blood sedimentation rate was within the normal range. I should also like to know if she had fever, but it is interesting that no comment is made about the temperature either here or later.

Dr. Mallory: The temperature was normal.

Dr. Bland: The next interesting thing about the blood examination is the 6 per cent eosinophilia, which is not high but a little higher than one ordinarily encounters. It is true that patients with rheumatoid arthritis at times run a mild eosinophilia. I think the arthritic clinic here has encountered an eosinophilia as high as 30 per cent without obvious explanation other than that the patient was suffering from rheumatoid arthritis.

The urine seemed to be all right, with the specific gravity perhaps a trifle low.

The first of a series of serious episodes occurred on the third hospital day at 12:30 at night, without obvious cause and without preceding cardiac symptoms. It consisted of rapid palpitation, — too rapid I think for a sinus tachycardia, — which makes me suspect that perhaps there was in progress at this time a tachycardia of ectopic origin, either auricular or ventricular. In general both are regular, but with experience one can occasionally detect on auscultation a slight irregularity with ventricular tachycardia. This slight tendency to irregularity with ventricular tachycardia can be observed more often in the electrocardiogram than recognized clinically. Fundamentally both types of ectopic tachycardia are regular.

Another prominent feature of this attack was "pain in the left chest." It would be helpful to know more about it. It apparently suggested heart pain because they tried nitroglycerin, without relief. The patient was in acute distress and in moderate shock. How long the attack lasted we do not know. It occurred in the early morning hours, and it usually takes some time for the house officer to arrive; however, he was able to make the above observations so I think it is fair to assume that the acute attack lasted at least fifteen minutes, possibly an hour or two. The electrocardiogram mentioned thereafter was almost certainly not taken until the following morning, some eight hours or more after the onset of this acute nocturnal episode. It showed evidence of rather marked left ventricular strain, which had presumably been present for some time. There was some evidence of coronary disease on the basis of the widening of the QRS complexes. The QRS complexes in Leads 2 and 3 were inverted. That means more than moderate left-axis deviation and makes us suspect early intraventricular block. It is evident then that the electrocardiogram was abnormal, but no comment is made at this time about the T waves. It may have been

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too early for the changes characteristic of acute myocardial infarction to have appeared, and besides the patient may not have had actual infarction of the heart the previous night, although a subsequent electrocardiogram and the clinical course strongly suggest it. What was the explanation of that attack then? We see patients of middle age or older with coronary disease who have angina pectoris during the course of paroxysmal auricular (or ventricular) tachycardia. It represents a "status anginosus," usually for the duration of the rapid heart action, dependent on underlying coronary disease plus a diminished output of the heart at the rapid rate. Whether this was only an attack of paroxysmal tachycardia with associated coronary pain or whether the patient actually had coronary occlusion or myocardial infarction we shall have to leave open for the moment. The subsequent course, as previously noted, strongly suggests that some permanent damage occurred in the myocardium at the time of this acute attack. It would be helpful at this point to know if the patient developed fever thereafter, if the blood pressure dropped, or if there was a leukocytosis.

She apparently was not in too bad a condition the next day, but on the third day thereafter she had a second, rather alarming episode. This time she suddenly lost consciousness for thirty seconds, and an associated tachycardia of 130 was noted. Following this she again seemed to be all right without residual neurologic changes. There are one or two possible explanations for this cerebral episode. It would seem to indicate a transient cerebral anemia, I should say, rather than structural damage to the brain. It lasted only thirty seconds, with no residual signs thereafter. What might do that? Cerebral anemia secondary to disturbed cardiac output seems most likely. The pulse was regular at 130. That rate suggests that the patient may have had another paroxysm of tachycardia, perhaps (but not probably) associated with a short period of ventricular fibrillation. High-grade heart block seems unlikely in view of the observed heart rate. I believe that this episode probably was not caused by an embolus. I cannot account for it on any other basis than that of a transient cerebral anemia.

We are then told that the blood pressure was considerably lower, with a diastolic reading of 60, and for the first time we find a comment on certain physical signs indicative of serious heart disease. The heart was enlarged. A loud blowing systolic murmur developed or at least became more prominent. It was thought that she had a slight systolic murmur in the past, but this was not commented on at admission. Dilatation of the heart alone may produce a fairly loud apical systolic murmur. In addition to the signs of enlargement there was present a gallop rhythm, which is reliable evidence at this age of serious myocardial weakness. The amphoric A_2 suggests one of three things: hypertension over a long period of time; marked aortic atherosclerosis without hypertension; or, as is thought by some, early syphilitic aortitis. With a negative Hinton test and no other suggestive evidence of syphilis, except possibly the pupils, I am willing to discard syphilitic aortitis from further consideration.

The next event which requires a passing comment was the pain in the legs following the use of splints, which I assume was due to the splints. No fever, no local tenderness and no swelling are mentioned. Therefore it is unlikely that this patient was developing a phlebitis, although in view of the lung signs later observed we must keep this possibility in mind. Examination of the heart at this time confirmed what had previously been noted with one additional finding, which is somewhat confusing—a short musical diastolic murmur which replaced the second sound. Ordinarily diastolic murmurs are not musical. They are usually blowing in character if of aortic or pulmonary origin and best heard at the base of the heart, and rumbling if of mitral origin and ordinarily best heard at the apex. It is unusual to hear an early diastolic murmur which replaces the second sound and yet is not audible at the base, because the murmur arises in association with either A_2 or P_2. Occasionally an aortic diastolic murmur may be heard better toward the apex than elsewhere, but this is exceptional; and, finally, when a diastolic murmur is heard at the apex, if we are uncertain about its origin and character, in the long run I think it most likely arises at the mitral orifice.

DR. MALLORY: For what it is worth to you, Dr. Bland, the initial physical examination, when the heart was described as negative, was done by a house officer. Dr. Howard B. Sprague heard a gallop rhythm and systolic murmur. Dr. Maurice Fremont-Smith described the systolic and diastolic murmurs at the last episode.

DR. BLAND: We are left somewhat in a dilemma. Did the cardiac murmurs actually appear under observation, or were they present and not mentioned at the time of admission? It makes a considerable difference which alternative we accept. We know that functional diastolic murmurs may arise during the course of cardiac dilatation, especially in children. This is certainly less common in older people, and I suppose it is safer to assume that this patient had slight scarring of the mitral valve dating back to childhood. Marked dilatation and weakness of the myocardium may

have produced a functional diastolic murmur at the cardiac apex or it may have been of aortic origin after all. The most important consideration, however, is that we have clear evidence of serious myocardial weakness manifested by the gallop rhythm and actual failure as shown by the dyspnea and medium coarse rales heard at both lung bases as high as the scapulas. I suppose we should also keep in mind pulmonary infarction, but the bilateral and basal distribution of the rales and the absence of fever in the face of clear evidence of serious weakness of the heart make this less likely than left ventricular failure.

The blood pressure had been rising a little, and then the patient suddenly developed complete anuria for twenty-four hours. That is a little difficult to explain. Dr. E. Ross Mintz has recently reviewed the experience at this hospital in connection with infarction of the kidney. The majority of renal infarcts are painless, and I asked him the other day if it were possible to have a complete suppression of urine from a renal infarct without pain. Such has been encountered. Another interesting point, according to Dr. Mintz, is that although most renal infarcts are associated with hematuria, the absence of hematuria does not necessarily exclude renal infarction. It does not seem likely that the patient's blood pressure was low enough to cause a cessation of renal function on that score alone. The diastolic pressure shortly thereafter was very good, and at no time when it had been recorded was it alarmingly low. I remain at somewhat of a loss to explain this acute anuria for twenty-four hours, unless it may have been secondary to renal infarction. Nothing is said about the findings in the urine and the blood thereafter, but the sequence of events suggests a slowly progressive left ventricular heart failure with probably a terminal element of renal failure.

From the general course of this patient's fatal illness it seems to me there are one or two things of which we can be reasonably certain and a few things about which we may raise a question. There seems no doubt about the chronic arthritis, probably of the rheumatoid type. Secondly, I think the evidence is sufficiently clear that the patient had hypertensive and coronary heart disease with congestive failure, chiefly of the left ventricle with probably a recent myocardial infarct. I should like to raise the question also as to whether this patient may have had slight mitral regurgitation of long standing, dating back to rheumatic fever in childhood, but perhaps not contributing significantly to the terminal illness. There was considerable uncertainty concerning the diastolic murmur, but there may also have been slight rheumatic scarring of the aortic valve; if present I do not believe that it contributed significantly to the terminal events. Finally, one wonders if this patient also had slight chronic vascular nephritis, with possibly renal infarction.

Dr. Joseph S. Barr: Before her entry to the hospital I saw this patient with Dr. Fremont-Smith with regard to the possibility of doing something about the arthritis. She had been a wheel-chair invalid for months, perhaps for a year or more. She had definite rheumatoid arthritis. The physical examination on admission is deficient because this disease was easily recognizable. Both knees, ankles, wrists and hands showed the typical fusiform joint swellings of proliferative arthritis. She was deaf and without her hearing aid could not hear at all, so it was difficult to get a history. She was a frail little person and I was not sure whether we could do anything for the arthritis but advised hospitalization for study to see what could be done. Between that time and her entry to the hospital she became worse, so that on admission it was obvious that the joints were secondary and the medical condition primary. After a hospital stay of two weeks I gave up any serious effort toward straightening the joints and she was transferred to the medical service.

Clinical Diagnoses

Rheumatic and hypertensive heart disease.
Angina pectoris.
Atrophic arthritis.

Dr. Bland's Diagnoses

Rheumatoid arthritis.
Hypertensive and coronary heart disease.
Myocardial infarction.
Congestive heart failure, chiefly left ventricular.
Slight rheumatic heart disease with slight mitral and aortic regurgitation?
Vascular nephritis?
Renal infarction?

Anatomical Diagnoses

Coronary thrombosis, old.
Cardiac infarction, old and recent.
Endocarditis, chronic rheumatic, with stenosis, mitral and aortic.
Rheumatoid arthritis.
Arteriosclerosis, moderate aortic and coronary.
Hydrothorax, slight, bilateral.
Chronic passive congestion of liver and kidneys.

Pathological Discussion

Dr. Mallory: The postmortem examination showed besides the generalized evidence of rheumatoid arthritis a group of cardiac lesions. She

did have old scarring of both mitral and aortic valves without, however, any marked degree of stenosis or insufficiency, but it was unquestionably a rheumatic lesion. The most important finding was an area of fresh infarction at the apex and a somewhat larger adjacent area of quite old infarction overlaid by heavy fibrous scarring which must have dated back months and possibly years. The descending branch of the left coronary artery was completely occluded with a fairly old thrombus, and we did not succeed in identifying any fresh thrombus to go with the recent infarct. That does not mean that it was not there. In cases of long-standing complete stenosis of a coronary artery, extensive collateral circulation develops and the thrombi must often be sought in unusual spots, so that unless one injects the heart they are easily missed. The kidneys were completely negative except for minimal vascular lesions. Nothing was found which would explain the anuria. The brain was grossly negative, and if there was an embolus, it must have been an extremely minute one which had not caused any recognizable softening.

A PHYSICIAN: Was there any pulmonary infarction?

DR. MALLORY: No.

CASE 25302

PRESENTATION OF CASE

First Admission. A twenty-year-old single Canadian was admitted complaining of right-sided headaches.

For three months before admission the patient suffered from intermittent headaches over the right side of his head, accompanied by a right nasal discharge. Three weeks before entry, following an attack of coryza, he suffered from violent pains in the right side of his face. His nose was markedly obstructed, and there was a discharge of yellow pus. This was soon followed by severe generalized headaches. Ten days before entry he had projectile vomiting without nausea and had two more attacks of vomiting before admission. His nasal discharge continued. Right nasal polyps were removed two days before entry. His past and family histories were noncontributory.

Physical examination showed a well-developed and nourished man in no acute discomfort. There was yellow purulent material in the middle nasal meatus, and the right middle turbinate was polypoid; the septum was markedly deviated to the right. None of the sinuses on the right would transilluminate. Those on the left transilluminated well. There was tenderness along the floor of the right frontal sinus. The pupils reacted sluggishly to light and not at all to accommodation. There was a limitation of upward ocular motion. The optic disks were blurred and elevated, the veins somewhat distended; there was less than 1 diopter of papilledema. A portable perimeter showed constriction of the upper fields. The ears were negative. There was a stiff neck, and bilateral positive Kernigs. The patellar reflexes were both very brisk, the ankle jerks normal. There was no Babinski sign.

The temperature was 97.4°F., the pulse 72, and the respirations 20.

Examination of the urine was negative. The blood showed a hemoglobin of 90 per cent, and a white-cell count of 9300 with 64 per cent polymorphonuclears. A blood Hinton test was negative. A lumbar puncture gave an initial pressure of 300 mm. of water. The spinal fluid contained 121 cells (11 polymorphonuclears and 110 lymphocytes) per cubic millimeter and had a total protein of 148 mg. per 100 cc., a sugar of 59 mg., a 4444455553 gold-sol curve and a negative Wassermann test. Several spinal fluid cultures showed no growth.

An x-ray film of the skull showed very slight separation of the sutures. There was considerable calcification in the pineal region.

On the day of admission the floor of the right frontal sinus was removed, and all the ethmoid cells taken out. The frontal sinus contained thick yellow pus under pressure, and the ethmoids were filled with a thick, dark mucous membrane. On the third hospital day the patient had projectile vomiting. Each fundus showed 2 diopters of papilledema. Associated ocular movements above the horizontal were absent, although he could raise the left eye upward alone. The pulse was 48, the respirations 12, and the temperature 98.6°F. The right frontal lobe was explored; this revealed a tense but otherwise normal dura. A needle was inserted 5 cm. in all directions, but no resistance or pus was encountered. On the sixth hospital day the patient was much improved. Vomiting ceased, there was no fever, and the pulse rose to 70. The neck, however, remained stiff, and there was considerable bulging of the operative incision. There was no leakage of cerebrospinal fluid. The patient continued to improve; on the ninth hospital day he had less than 1 diopter of papilledema and could look upward, and the pupils reacted to light and accommodation. During the next seven days he again developed signs of increasing intracranial pressure. There was diplopia on looking to the left, which increased on looking downward and to the left, the right eye remaining higher and not moving so far to the left. There were about 4 diopters of papilledema on the right, less on the left. A lumbar puncture on the nineteenth day showed an initial pressure

of 400 mm. The fluid contained 12 white cells and 8 red cells per cubic millimeter, a total protein of 134 mg. per 100 cc., a sugar of 54 mg. and chlorides of 707 mg. During the next four weeks he improved progressively and there were no further headaches or vomiting. The papilledema reduced to 1 diopter or less. He acted normally. On the fortieth hospital day a lumbar puncture gave an initial pressure of 320 mm. There were 35 lymphocytes per cubic millimeter, and a protein of 154 mg. per 100 cc. He was discharged on the forty-eighth hospital day.

Second Admission (six months later). The patient's condition had been good, although he had had occasional attacks of diplopia and was somewhat nearsighted. There had been no headaches or other central-nervous-system symptoms. He had gained 43 pounds in weight.

Examination was essentially negative except for nasal polyps and a deviated nasal septum. His vision was 20/20 bilaterally.

The septum was partially resected, and he was discharged on the tenth hospital day.

Third Admission (two weeks later). One week after discharge he began having pains in the back of his head and neck, which caused him to draw up his hands and arms. There were no real headaches, and he had not vomited.

On physical examination the pupils were equal, dilated, and did not react to light. There was a 1.5-cm. pulsating hernia at the lower end of the old frontal operative scar. The blood pressure was 120 systolic, 80 diastolic.

The temperature was 97.5°F., the pulse 73, and the respirations 20.

Examination of the urine was negative. The blood showed 85 per cent hemoglobin, and a white-cell count of 9300.

On the second hospital day the hernia was removed, and the skin edges sutured together. On the sixteenth hospital day it was shown that diplopia on looking to the left and down was still present. His recovery from the operation was uneventful, and he was discharged on the seventeenth hospital day.

Final Admission (four months later). Two months before admission, following an automobile drive, he stopped suddenly on entering the house, turned his head far to the left, fell, and remained unconscious for twenty-five minutes. He suffered no injury. His limbs and body were extended and rigid, his eyes open and fixed straight ahead. He bit his tongue and a clothespin was inserted in his mouth. There was no incontinence. Following the attack he felt well and did not remember the event. He remained well until eleven days before entry when a severe pain suddenly occurred in the back of his head behind the right ear. The pain was very sharp but lasted only a few seconds. He then had intermittent pain and buzzing in the right ear, as well as intermittent headaches until entry. The pain in the ear was relieved by heat, but his headaches were only slightly relieved by aspirin and Anacin. About twenty minutes after breakfast on the day before admission he vomited. He had been drowsy for the previous ten days but had always been rational. No further seizures had occurred. He had continued to gain weight.

Physical examination showed an obese man in acute distress from time to time because of pain in back of the head and neck. Pains recurred every one to five minutes during the examination and lasted two to five seconds. He cleared his throat occasionally, raising yellow blood-streaked sputum. The eyes were at different levels, the right being lower than the left and showing an intraorbital fullness. Tenderness was present over the occipital region, most marked over the right mastoid. The ears showed no abnormality. The blood pressure was 118 systolic, 80 diastolic. On neurological examination the pupils were small, equal and did not react to light or accommodation. There was a fine lateral nystagmus, and upward gaze was definitely limited, the left eye moving higher. There was slight bilateral ptosis of the lids. The disks were blurred. No gross visual field defects could be discerned. There was slight right facial weakness. The finger-to-nose test was more hesitant and inaccurate on the right than the left. The tendon reflexes were active and equal. Bilateral Babinski signs were present. There was unsustained ankle clonus bilaterally. The remaining neurological examination was negative.

The temperature was 100°F. rectally, the pulse 71, and the respirations 25.

Examination of the urine showed a trace of acetone but was otherwise negative. The blood showed a red-cell count of 4,700,000 with 100 per cent hemoglobin, and a white-cell count of 12,200 with 85 per cent polymorphonuclears. A lumbar puncture gave an initial pressure of 430 mm., and the final pressure after withdrawing 10 cc. was 180 mm. The fluid was clear and colorless. There were 24 lymphocytes per cubic millimeter. The total protein was 164 mg. per 100 cc., the sugar 71 mg. The gold-sol curve was 5555552110.

X-ray films of the skull showed no evidence of osteomyelitis at the operative defect. The sella turcica was increased in size, and there was marked erosion of the posterior clinoids and dorsum sellae. The pineal gland showed extensive calcification, and by measurement was displaced backward and downward.

On the second hospital day a ventricular tap through the right frontal lobe resulted in the escape

of 50 cc. of clear fluid under high pressure at a depth of 3 cm.

After ventricular injection of air there was a large amount of air in the lateral and third ventricles. The ventricles were grossly dilated, the right lateral slightly more than the left. The third ventricle was dilated, and there was no evidence of air entering the aqueduct of Sylvius or fourth ventricle. On the fourth hospital day a Stoakey operation was done; this exposed the chiasm, and a thin-walled third ventricle was opened. No definite lesion was found. Following the operation the temperature mounted to 106°F. and remained close to that level for forty-eight hours. A lumbar puncture on the fifth hospital day gave an initial pressure of 210 mm.; the fluid was slightly bloody. The temperature continued at 101 to 105°F.

On the fifteenth hospital day there were dullness and fine rales over the right base. Chest x-ray films showed the mediastinum shifted slightly toward the right. The right diaphragm was high, and there were linear areas of density extending from the hilus down to the posterior portion of the lower lobe. A lumbar puncture gave an initial pressure of 240 mm. The fluid was clear and xanthochromic. There were 92 red cells, 4 lymphocytes and 10 polymorphonuclears per cubic millimeter. The total protein was 124 mg. per 100 cc., and the chlorides 801 mg. He failed rapidly and died on the seventeenth hospital day.

Differential Diagnosis

Dr. Harry C. Solomon: I saw this case for a week before I went on vacation. The patient was referred from the Massachusetts Eye and Ear Infirmary with a story of intermittent headache prior to admission; he had a good deal of nasal discharge of yellow pus, almost exclusively from the right side of his nose. Before entry he had had projectile vomiting. When he came in the sinuses on the right side were quite obviously filled with pus. There were a number of signs indicating that he had an intracranial disorder. The first one was, of course, that there was some increase in intracranial pressure as shown by ophthalmological examination; however, the signs were not marked. He also had a stiff neck. Those factors taken together suggest that he had an extension of infection from the sinuses into the intracranial cavity. A striking neurological finding was that he had limitation of upward movement of the eyes; this suggests at once that he had something in the region of the third ventricle because that is the usual site of a lesion which produces this symptom. Examination of the body as a whole showed nothing else. A lumbar puncture confirmed what we have surmised from the projectile vomiting and elevated optic disks, namely increased pressure (300 mm.). There were 121 cells per cubic millimeter. Adding together the sinus infection, the stiff neck, the cells in the spinal fluid, and the evidence of increased intracranial pressure we have very suggestive evidence for abscess. The high total protein and strong gold-sol reaction go with such a diagnosis, as well as a sugar that was not particularly low. The sugar is important and makes meningitis relatively unlikely.

X-ray films of the skull gave no further evidence of importance, though the slight separation of the sutures suggests that the pressure had been elevated for a fairly long time. At that time there is no statement regarding displacement of the pineal gland to throw light on where the expanding lesion might be found. Despite the fact that there was limitation of upward motion of the eyes, which throws attention backward to the middle fossa and makes us wonder about extension of infection from the sphenoidal sinus, operation on the frontal sinus was performed; the posterior wall of the sinus was removed and nothing was found suggesting an abscess, even though the frontal lobe was quite well explored by needle. In the meantime things were progressing rapidly because the papilledema continued to increase markedly. There was a tense dura as further evidence of increased pressure.

Next, he began to develop diplopia on looking to the left side, a disturbance or paralysis of the right external rectus muscle, which might well be merely a pressure symptom. Further, lumbar puncture on the nineteenth day showed a pressure increased over what it was before, — 400 mm. with 12 white cells, — but for some reason he then began to improve. Despite the fact that the pressure remained high (320 mm.) and the fluid still showed 35 lymphocytes and a high protein, he was discharged at the end of forty-eight days, I believe without a definite diagnosis' having been made, although I am not sure of that. At any rate no further operative procedure was undertaken and he went out relieved of symptoms. Whether that was in part because he had a small decompression, one can only guess. Abscess will do that sort of thing, — improve spontaneously, — but so will tumor, and so will a condition that we often call, for lack of a better term, pseudo-tumor, a condition of which no one knows the etiology but from which decompression gives relief.

He returned to the hospital six months later for some reason. During these six months he had been feeling well except for occasional attacks of diplopia evidencing that something was still going on, and we wonder whether the whole thing was some odd form of encephalitic process with interference of outflow of cerebral fluid from the base,

and increased pressure on that basis, together with some other vague encephalitic foci in various other places to give the symptoms he continued to have. A striking fact is that in six months he gained 43 pounds in weight. That suggests a metabolic disturbance and makes one think of something related to the pineal gland. We have no previous note as to the location of the gland by x-ray, nor have we the report on this admission. At any rate he had a resection of the septum and left the hospital on the tenth day.

Two weeks later things happened. He began to have pain in the back of his head and neck, which caused him to draw up his hands and arms. We find that he had some herniation in the frontal region where a piece of the skull had been removed. He still had diplopia on looking upward. It was found he had disturbance of the visual fields. Probably there was some loss of the upper portion of the fields and that is not readily explained. A lesion around the geniculate ganglion might produce such a change, or a lesion in the floor of the anterior fossa pressing on both optic nerves; but it is not a good clinical symptom on which to rely, and for practical purposes the best thing to do is to forget it. After the third admission he went out and got along well for two months, when he had a seizure in which his eyes and head turned to the left. He probably had something in the way of cortical irritation; although the lesion may have been in the brain stem. At any rate he had a convulsion and recovered. Then he was better again for a while.

Eleven days before his final entry to the hospital some new symptoms began. He had severe pain in the back of his head behind the right ear, with intermittent buzzing as well as pain and generalized headaches. That again is quite definite and implicates the eighth nerve. On examination he was found to be having sharp paroxysmal pain occurring at intervals of one to five minutes and lasting two to five seconds. That is hard to explain. At any rate he still had what had been present more or less all the time — signs and symptoms that implicated the region of the middle fossa in the midbrain region. His third nerve was definitely involved. Once more the pupillary changes and inability to raise his eyes upward suggest something of a midbrain localization of the trouble.

When he came in this last time there was lateral nystagmus, which might be a pontine disturbance. There was a bilateral ptosis, again suggesting something in the neighborhood of the third nerve. There was right facial weakness, suggesting brain-stem involvement, and he had developed bilateral Kernig signs which also could be accounted for by new growth of one sort or another in the pontine midbrain region. The spinal fluid pressure was still very high (430 mm.), and on withdrawal of 10 cc. it only dropped to 180 mm., suggesting a large reservoir of fluid from which to draw; so one suspects that he might have had a hydrocephalus. There were 24 lymphocytes, a finding which again suggests irritation. It might be abscess or tumor or cyst or something near the ventricular surface. There was no evidence of osteomyelitis, and I think we have ample reason to forget the possibility of frontal abscess.

The x-ray then began to show something that seemed to localize the lesion quite well. The pineal gland was pressed backward and downward so that there seemed to be a lesion above and in front of it. The sella turcica showed erosion of the posterior clinoids and dorsum; this again suggests something above and behind, therefore giving rise to the thought that the lesion lay somewhere in front of the pineal gland and behind the sella. So we think of a disturbance around the aqueduct of Sylvius, above it and pressing down on it. Then the ventricular tap showed marked hydrocephalus, a very thin cortex and large ventricles. Air injection showed large ventricles, but no air going back of the third ventricle, which might be due to technical difficulties, as it is sometimes difficult in a ventricular air injection to get the air to go back as far as one wants. On the other hand with marked dilatation everywhere else one still thinks that there was something behind the third ventricle that stopped it. Of course that could be a ball-valve type of tumor in the region of the aqueduct of Sylvius or the posterior portion of the third ventricle; this would account for the remissions and then the new symptoms. At any rate, apparently as a result of the ventriculogram an attempt was made to find the lesion in the third ventricle or posterior to it. Therefore the ventricle was opened without, however, any success.

The final thing that comes to our attention is the x-ray film of the chest in which the right diaphragm was high suggesting that there was something in the liver. In actual practice in the hospital we should go down to the x-ray room and get a complete and usually satisfactory answer as to what that meant. I do not know whether Dr. Holmes is going to tell me what that really means.

DR. A. THORNTON SCOTT: The patient had a friction rub at the base at the axilla on the right, and two days before death the right leg was swollen.

DR. GEORGE W. HOLMES: I cannot add anything regarding the skull films. I might expand a little on the question that has been raised about the chest. The diaphragm is a little high on both

sides but more so on the right than on the left, and the angle between the diaphragm and the chest wall is obscured on that side. I should suspect that the trouble was in the patient's chest rather than in the liver or below the diaphragm. I cannot rule out the liver, but it seems to me more likely that he had a pneumonic or pleuritic process in the chest rather than anything in the liver.

Dr. Solomon: Coming back to the head, the lesion from the standpoint of localization was definitely back of the third ventricle. The problem is, What was it? I do not believe it was in the pineal gland itself because the gland was displaced. So he had a lesion in that general region which apparently was an expanding one; it was not an abscess, not inflammatory but may well have been a tuberculoma or glioma. On the basis of possible liver enlargement I wondered whether we were dealing with some form of cyst, perhaps one due to the echinococcus, but now the best that I am able to suggest is that he had a lesion behind the third ventricle in the midline pressing downward, probably either a tuberculoma or glioma, possibly a cystic lesion that occasionally grew smaller or larger giving different pressure effects.

Dr. Henry R. Viets: Do you associate his difficulties at the time of the last entry with the first-admission symptoms of sinus infection and, possibly, meningeal irritation or abscess?

Dr. Solomon: No; I have discarded the idea of abscess, although that is still a possibility. I think that the so-called meningeal irritation was due to increased pressure in that region.

Dr. Gustave B. Fred: When I first saw the patient he complained of headache, vomiting, stiff neck and a creamy discharge from his right nostril. He did not have failure of upward gaze.

X-ray studies presented evidence of a right frontal sinusitis. Spinal puncture revealed increased pressure and high cell count. For fear of an impending meningitis I performed an external right frontal sinus operation and found creamy pus with markedly thickened mucous membrane in the sinus. I left the incision wide open. Two days later failure of upward gaze was noted and his other symptoms were aggravated. I made a diagnosis of a brain abscess in the right frontal lobe, which was confirmed by Dr. James B. Ayer. I explored the right frontal lobe, but no abscess was found. Later a consultation was held with Dr. Ayer and Dr. Charles S. Kubik, and the question of pineal-body tumor was suggested. I was on the verge of transferring the patient to the Neurosurgical Department for exploration when he suddenly became well, as I thought. He was discharged home. The third and fourth admissions to the hospital were for plastic work on the original external incision, which had been left open at the time of the first operation. I saw him a year after my original operation and advised admission to the hospital. The last operation was done in the Neurosurgical Department.

Clinical Diagnoses

Midbrain tumor.
Pulmonary infarction.

Dr. Solomon's Diagnosis

Midbrain tumor.

Anatomical Diagnoses

Pinealoma.
Internal hydrocephalus.
Thrombophlebitis, right femoral vein.
Pulmonary infarction, bilateral.
Obesity.
Abdominal striae.
Operative wounds.

Pathological Discussion

Dr. Charles S. Kubik: There was, as Dr. Solomon suspected, a tumor of the midbrain. This was a small infiltrating growth, measuring approximately 2 cm. in diameter, situated in the tegmen and extending forward to the region of the third-nerve nuclei and practically obliterating the aqueduct. The greater part of it was on the left side.

The tumor was a pinealoma. It was composed of large rounded, polyhedral and elongated cells with well-stained cytoplasm, the nuclei containing strikingly large nucleoli. Within the tumor and also the adjacent perivascular spaces and subarachnoid space there were lymphocytes and a fair number of plasma cells. This infiltration of the tumor with lymphoid cells is characteristic for this type of pinealoma, and the meningeal infiltration in this case probably accounts for the cells found in the cerebrospinal fluid during life.

The opening into the third ventricle was patent, providing a communication between the ventricles and the subarachnoid space. Comparing the postmortem findings with the encephalogram there seemed to be a considerable diminution in the size of the ventricles; this indicates without much doubt that ventriculostomy had relieved the internal hydrocephalus.

Dr. J. H. Means: Is this type of tumor radiosensitive?

Dr. Kubik: I am not sure that the cases of pinealoma or suspected pinealoma responding to radiation have been checked by biopsy.

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FACTUAL DATA

Two documents recently issued by the American Medical Association deserve more than casual attention from the many now interested in medical economics. Those motor-minded individuals who have been annoyed by so many surveys will be pleased with the action presented in the one hundred and eighty-five page pamphlet issued by the Bureau of Medical Economics entitled *Organized Payments for Medical Services*. The material on which this publication is based has been collected over a long period of time and includes data concerning all kinds of prepayment plans, from those of the fraternal organizations of years ago down through the most recently operated services sponsored by the Farm Security Administration and by various medical societies. Commercial insurance companies alone now pay out approximately $300,000,000 annually in cash indemnities to assist in the payment of medical bills. Reading this it would appear that no responsible person need go without an opportunity to budget his medical expenses. The rare burden incurred by consecutive months of hospitalization is not so well provided for, however. People may still be rendered destitute by certain types of injury or chronic disease, but this is a problem of economic circumstances rather than one concerning the provision of adequate medical service.

The other publication, *Factual Data on Medical Economics*, is a graphic collection of information from reliable sources concerning physicians, populations, hospitals, community incomes and various ratios between these items. Death rates in this and other countries and for various diseases are stated and charted with little more than a running description of text, and even this largely refrains from interpreting the data presented. It is printed on sixty-eight pages, 8 by 11 inches in size, and contains twenty-five tables and twenty-nine charts. The sort of information is given with which the medical profession is, or should be, familiar, but it is also in a form that the general public can readily understand. Too often, popularized material sacrifices accuracy to ensure clarity, but in this booklet no such exchange of values has occurred. With a heavier cover it would be suitable for, and would find many interested readers in, the doctor's waiting room. It should be in the minds of all who contemplate future activity in the framing of legislative policies and acts.

SYPHILIS AND THE LAW

The recent article by Stokes and Ingraham* on "Syphilis and the Law" emphasizes not only the new wave of legislation in the genitoinfectious disease field, but also the need for the co-operation and the influence of the physician in matters pertaining to this problem. The authors point out that laws relating to the control of syphilis should

*Stokes, J. H., and Ingraham, N. R., Jr.: Syphilis and the law; with a discussion of the false positive blood serologic test. J. A. M. A. 112:1133-1143, 1939.

take account of the great variability in individual cases and the necessity for expert medical interpretation in many instances. Any law should therefore be drawn in sufficiently general terms to allow for the exercise of individual expert medical judgment as occasion arises. They point out the fallacy of depending on a single test or procedure without adequate control in the diagnosis of syphilis, and they discuss at length the false-positive serological test and the numerous injustices arising in the interpretation of such a test without adequate experience and qualifications.

Numerous states have recently enacted laws concerning the genitoinfectious diseases, with regard to marriage, blood donors, food handlers and other industrial groups. Other states have similar laws under consideration. Such laws are justly concerned with revealing contagious syphilis, but it is a grave question as to the attitude which the courts will take when these laws begin to reveal, with reference to relatively prominent individuals, infections by diseases which are in no way transmissible. It is true that most legislation aims at the discovering of the disease, regardless of whether or not it is infectious, but it is also true that it is difficult to maintain absolute secrecy regarding reports. Another question which will undoubtedly be presented to the courts is the matter of excluding employees from work because of a noncontagious syphilitic infection.

On the statute books there are many laws enacted especially in regard to health matters which have resulted in confusion and injustice, to say nothing of the inability to enforce them. All laws should be an expression of educated public demand, and in attempting to enact any particular health laws it is essential to carry out an intensive application of educational methods through the press, through medical authorities, through public-health agencies, and perhaps best of all, through correctly educated patients. It would seem that the model laws for the control of syphilis that were prepared by the American Social Hygiene Association some years ago should be examined in the light of recent surveys and that an attempt should be made to progress not only toward some such general law but also toward more uniform legislation in the various states. But in addition there should be an educational accompaniment to all such legislation — education in various phases of the disease to the lay public, to the physicians and to each individual patient. This legal phase demands the interest of the whole medical profession. Not only is the interest required, but it is the duty of physicians to co-operate and to influence the enactment of rational statutes which will consider the whole problem in the light of modern knowledge of the disease. In the attempt to control syphilis by law there are three essential features: first, the insistence on an adequate examination, as well as on a laboratory procedure; second, the preservation of the opportunity for individual medical interpretation by properly qualified physicians in the complex problems which arise; and, third, an adequate educational campaign over a period of years.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

COMPLETE INVERSION OF THE UTERUS

Mrs. A. M., a twenty-year-old primipara, was delivered normally at term on April 9, 1939.

Her family history was unimportant. The patient had never been seriously ill. Catamenia began at twelve, were regular with a twenty-eight-day cycle and lasted four days without pain. Her last period was July 8, 1938, making her expected date of confinement April 15.

Her pregnancy had been normal throughout. Labor started at 3 a. m. on April 9, and she was delivered with low forceps at 12:52 p. m. after a second stage of an hour. The placenta separated spontaneously and came away with gentle manipulation at 1 p. m. The patient bled profusely after the delivery of the placenta and membranes, and an ampule of Ergotrate was given; as the bleeding continued, the vagina was firmly packed. A lateral episiotomy was repaired. One thousand cubic centimeters of 10 per cent glucose in saline

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

was given intravenously, and the fundus was held constantly without pressure. Two hours after delivery the blood pressure had dropped from 132 systolic to 92 systolic, 60 diastolic, and the pulse ranged from 120 to 130. Another 1000 cc. of 10 per cent glucose, this time in distilled water, was given, and preparations were made for transfusion.

The patient was seen in consultation at 5 p. m., at which time she was being given a direct transfusion of 500 cc. of her husband's blood, to which she reacted well. On palpating the fundus, the customary rounded dome seemed to be slightly depressed at its central point, although as a suprapubic mass could be felt nearly up to the umbilicus, it was not thought that the uterus was inverted. When the transfusion was completed, the patient was examined vaginally under nitrous oxide and ether anesthesia.

On examination the fundus was felt to be completely inverted into the vagina, with the cervix moderately contracted around it. With one hand on the suprapubic region and the other hand doubled into a fist in the vagina, steady upward pressure was exerted by the vaginal hand. The inverted fundus could be felt to rise slowly through the cervical ring. During this procedure the anesthetist reported that the patient had stopped breathing and was pulseless, but as the fundus was all but replaced, pressure was continued and the uterus returned entirely to its normal position. When replacement was complete, the condition of the patient immediately improved. A firm vaginal packing was inserted and the patient left the operating room in fair condition. At 9:45 p. m. she was given a second direct transfusion of compatible blood.

The packing was removed the next day without further bleeding. The fundus remained in its proper position and involuted normally. No elevation of temperature occurred, and convalescence was uneventful. The patient and her baby went home in good condition on the thirteenth postpartum day.

Comment. This case represents the postpartum hemorrhage that is so characteristically associated with inversion of the uterus. Apparently the inversion existed for about five hours before recognition, yet at that time the replacement of the inverted uterus was accomplished without any difficulty. Vaginal packing, although done in this case without appreciating its logic because the diagnosis of inverted uterus had not been made, can and does control hemorrhage from this condition because the gauze is intimately pressed against the inverted, exposed sinuses. Again the value of transfusion is emphasized, and once more the absence of infection even when the uterine sinuses have been traumatized is worthy of note. Cases of this type illustrate the importance of an early diagnosis; if such can be made and reposition of the fundus accomplished, serious sequelae seem to be unusual.

DEATHS

CARLISLE — FRANK H. CARLISLE, M.D., of Wellesley, died July 20. He was in his sixty-first year.

Dr. Carlisle received his degree from the Harvard Medical School in 1904. Soon after his graduation he became associated with the Foxboro and Norfolk state hospitals as assistant superintendent and later became medical director of the Bridgewater State Hospital.

He was a fellow of the Massachusetts Medical Society and the American Medical Association and was a member of the American Psychiatric Association and the New England Society of Psychiatry.

His widow, two sons, his mother, a sister and a brother survive him.

MURRAY — P. JOSEPH MURRAY, M.D., of Dorchester, died July 19. He was in his sixty-fourth year.

Dr. Murray received his degree from Boston University School of Medicine in 1908. He was a former member of the Massachusetts Medical Society.

MISCELLANY

NOTES

Dr. Lawrence J. Henderson, Lawrence Professor of Chemistry at Harvard University and professor of biological chemistry at Harvard Medical School, will deliver the next Pilgrim Trust Lecture in London, under the sponsorship of the Royal Society.

The following appointments to positions at the Harvard Medical School have been recently announced: Waldo E. Cohn, of Berkeley, California, research fellow in medicine, Ph.D. University of California '38; Roger S. Downs, of Saratoga Springs, New York, research fellow in medicine, M.D. Harvard '36; Alexander W. Souter, of Boston, research fellow in medicine, M.B., Ch.B. (hon.), University of Aberdeen '37; Justin M. Hope, of Iowa City, Iowa, research fellow in neuropathology, M.D. Pennsylvania '34; Victor Rudomanski, of Hearny, New Jersey, research fellow in pediatrics, M.D. Long Island College of Medicine '34; John B. Burrett, of Ann Arbor, Michigan, research fellow in physiology, M.D. New York Medical College '37; Horace O. Parrack, of New York City, research fellow in physiology, A.M. Columbia '32; William W. Beckman, of Boston, assistant in medicine, M.D. Harvard '35; Margaret E. M. Glendy, of Boston, assistant in pediatrics, M.D. University of Virginia '31; Nathan B. Friedman, of Chicago, Lucius N. Littauer Fellow in Pathology, M.D. Cornell '34; Joseph Fischmann, of New York City, research fellow in surgery, M.D. University of Berlin '26.

REPORTS OF MEETINGS

NEW ENGLAND OTOLARYNGOLOGICAL SOCIETY

The following are abstracts of papers presented at the April 12 meeting, in Boston, of the New England Otolaryngological Society:

LATERAL SINUS PHLEBITIS: EFFECT OF SULFANILAMIDE. Dr. F. M. Wattles, Boston.

A twelve-year-old girl was admitted to the hospital with a diagnosis of an acute right otitis media with mastoiditis. The pathogenic organism was a hemolytic streptococcus. A simple mastoidectomy was performed on the eleventh day after the onset of the otitis. A large mastoid was found with generalized destruction and pus throughout all the cells. Small areas of the lateral sinus and dura were exposed and found to be normal. Two days after the operation the patient had a chill, the temperature rising to 105.5°F. The mastoid wound continued to discharge hemolytic streptococci. A blood culture taken at the time of the chill was negative. Sulfanilamide was given: 170 gr. during the first twenty-four hours, followed by 80 gr. for each subsequent day. After three days of this treatment the patient showed no improvement. Blood cultures remained negative. Six days after the operation the right internal jugular vein was ligated, the mastoid revised, the lateral-sinus plate removed, and the sinus opened. Free bleeding was obtained from both ends, but the sinus wall showed marked phlebitis. Sulfanilamide treatment was continued for eight days, and the patient made an uneventful recovery. This case was cited to illustrate the fact that sulfanilamide did not inhibit the infection of the lateral sinus once it had begun. The desired result was obtained here by surgery. Surgical principles apply as much today as they did before the advent of sulfanilamide.

Discussion. Dr. Oliver Lothrop cited a similar case in which extensive mastoid destruction occurred despite adequate doses of sulfanilamide. Dr. Philip E. Meltzer stressed the necessity of removing all foci before instituting sulfanilamide treatment.

THYROXIN TREATMENT IN OTOSCLEROSIS. Dr. J. E. Quincy. Boston.

Referring to the work of the late Dr. A. A. Gray, of London, England, the author reported a series of 6 cases of otosclerosis treated by the injection of thyroxin into the middle ear. The following results and conclusions were given:

1. Objective improvement was noted in only 1 case.
2. Subjective improvement in well-being, as well as in hearing, was reported in all but 1 case.
3. Normal secretion of wax returned in 3 cases.
4. Tinnitus was relieved in 3 cases.
5. The maximum beneficial effect came on within four to eight days.
6. In all probability the course of treatment has to be repeated at intervals of six months to one year.
7. More improvement may be expected in the age group between twenty and thirty, since the process has not been going on so long as it has in older individuals.

From this report, the speaker believes that the procedure is worth while insofar as the improved feeling of the patient is concerned. It has been suggested that a control series be run wherein sterile water is used in place of thyroxin.

Discussion. Dr. G. H. Poirier said that most patients with otosclerosis feel better after almost any treatment. Dr. Quincy admitted that the "psychology of medicine" is strong, but said that he did not believe that the mere local application of thyroxin is sufficient to stop the progress of the disease.

THREE CASES OF LABYRINTHITIS. Dr. Philip Mysel, Boston.

These 3 cases had several features in common: (1) all had chronic otitis media of long standing; (2) all had large cholesteatomas; (3) all had marked bony destruction amounting to "nature's radical"; (4) 2 had fistulas in the horizontal canal, and 1 fistulas in the horizontal and the posterior canals.

The first case, that of a woman of forty-seven years, was admitted with symptoms of meningitis. The diseased ear showed no vestibular or cochlear function. Labyrinthectomy was done and within three or four days all meningeal symptoms disappeared. In the author's opinion this patient probably had had circumscribed labyrinthitis for a long time, the last attack having resulted in acute destruction of the labyrinth.

The second patient, a nine-year-old boy, was admitted with an acute exacerbation of an old chronic otitis. He had had vertigo for two days, with no chills but a high temperature and marked postaural pain, tenderness and swelling. The neurological examination and the blood cultures were negative. The mastoid process was found to consist merely of a thin shell filled with cholesteatomatous tissue. A large amount of this material was also removed from the middle ear. The horizontal canal showed a good-sized fistula. The operation was then stopped because the patient did not handle his anesthesia well. That same afternoon he developed a strong labyrinthine nystagmus to the good ear, without nausea, vomiting, headache or neurological symptoms. The cerebrospinal fluid showed no cell increase. The nystagmus persisted for over two weeks. About two and a half weeks later the middle ear was cleaned out, and the postaural wound closed. The labyrinthitis in this case was, in the author's opinion, induced by the removal of the infected cholesteatomatous material about the fistula. The acoustic function had never disappeared completely.

The third case, that of a boy twelve years of age with a history of chronic otitis media since infancy, was admitted with vertigo and headache of a few days' duration. A large cholesteatomatous cavity was shown by x-ray. There was a first-degree nystagmus to the good ear, otherwise the neurological examination was negative. Perception for whisper was lost completely, but conversation was heard at 4 feet. The following day the nystagmus became more marked and the patient developed a stiff neck. The temperature rose to 102°F. Lumbar puncture showed 1124 cells per cubic millimeter, 83 per cent of which were polymorphonuclears. In performing a radical mastoidectomy Dr. Poirier found two fistulas, one in the horizontal, the other in the posterior canal. The temperature came down within forty-eight hours, and the patient made an uneventful recovery. The author believes that the patient had an acute diffuse labyrinthitis secondary to an old circumscribed one. The meningeal signs and the lack of any other condition that could have explained the cells in the spinal fluid might have induced some surgeons to have done a labyrinthectomy. However, the patient promptly recovered after the middle ear had been cleaned out.

Discussion. Dr. Meltzer asked if it would not have been safer to have opened the labyrinth in the third case because of the meningeal symptoms. Dr. Mysel answered in the affirmative. He said that no physiological test of labyrinthine function should take precedence over the clinical evidence of meningitis, and pointed out that the

recognition of this fact plus a timely labyrinthectomy has lowered the mortality from 75 to 18 per cent. On the other hand labyrinthitis in itself does not call for operation unless there is a threatened intracranial complication. Dr. Poirier did not agree with the speaker. He believed that the boy would have gotten well without labyrinthectomy and that such an operation might have resulted in a meningitis.

SUPPURATION OF PETROUS APEX. Dr. L. E. White, Boston.

The patient, a woman of thirty-four, had a left simple mastoidectomy on January 15, 1939. Recovery was uneventful and on February 4 the postaural wound was healed. Five days later the patient was readmitted with a chief complaint of severe trifacial neuralgia and headache of three days' duration. Three days after the second admission a left postaural swelling was incised and drained. X-ray films showed pansinusitis and a negative petrous apex. Lumbar puncture was negative. A consultation with the nerve department reported: trigeminal neuralgia; epilepsy; psychoneurosis. A dental x-ray film showed an abscessed left lower bicuspid. The mastoid was revised. The dura was widely exposed for possible epidural abscess. There was soft bone above and below the horizontal semicircular canal. No lead to the petrous apex was found. An x-ray film taken five days later showed destruction of the petrous ridge on the left side. The petrous pyramid was drained, and a Mosher basket drain inserted. The latter was removed at the end of the sixth day. A subsequent film showed that the basket drain had given rise to a marked tunnel effect.

While this case was being presented, Dr. MacMillan showed and discussed the x-ray films taken at various periods of the patient's illness.

Discussion. Dr. Poirier said that he had had a similar case in which he used a rubber drain. Drainage was difficult, however, and the patient died of meningitis.

DISEASES OF SINUSES, MASTOIDS AND ESOPHAGUS FROM AN X-RAY STANDPOINT. Dr. A. S. MacMillan, Boston.

This was an exhaustive and splendidly prepared discussion of every phase of otolaryngology falling within the scope of the roentgen-ray specialist. The discussion centered around more than three hundred lantern slides of x-ray films. The various positions employed in the study, especially of the petrous pyramid, were discussed in detail.

NOTICES

ANNOUNCEMENT

WINTHROP F. WATTS, M.D., announces the opening of an office at 2 Brookhouse Drive, Marblehead.

REMOVAL

BENJAMIN ALPORT, M.D., announces the removal of his office from 1695 Main Street, Springfield, to 333 Bridge Street, Springfield.

INSTITUTE AT UNIVERSITY OF WISCONSIN MEDICAL SCHOOL

The University of Wisconsin Medical School announces an Institute for the Consideration of the Blood and Blood-Forming Organs to be held at Madison on September 4, 5 and 6.

Formal lectures will be given each morning and the early part of the afternoons of September 4 and 5. The latter parts of these afternoons will be devoted to round-table discussions, and in the evenings, addresses of more or less general interest are scheduled.

Those participating in the institute include: Drs. George R. Minot and Louis K. Diamond, of Boston; Drs. C. P. Rhoads, Paul Reznikoff, J. Furth and Claude E. Forkner, of New York City; Dr. E. B. Krumbhaar, of Philadelphia; Dr. Harry Eagle, of Baltimore; Dr. Charles A. Doan, of Columbus, Ohio; Dr. Russell L. Haden, of Cleveland; Drs. Hal Downey and C. J. Watson, of Minneapolis; Dr. Edwin E. Osgood, of Portland, Oregon; Prof. C. A. Elvehjem, of Madison, Wisconsin; Dr. L. J. Witts, of Oxford, England, and Dr. E. Meulengracht, of Copenhagen, Denmark.

The Wisconsin Alumni Institute has made available the funds necessary to finance the institute.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

There will be no Consultation Clinics for Crippled Children in Massachusetts during the month of August.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, January 6, 1940, at 2:00 p. m. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held in June, 1940.

Applications for admission to Group B, Part I, examinations must be on file in the secretary's office not later than October 4, 1939.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire board, meeting in Atlantic City, New Jersey, on June 8, 9, 10 and 11, 1940, immediately prior to the annual meeting of the American Medical Association in New York City.

Applications for admission to Group A, Part II, examinations must be on file in the secretary's office not later than March 15, 1940.

After January 1, 1942, there will be only one classification of candidates, and all will be required to take the Part I examinations (written paper and case records) and the Part II examinations (pathological and oral).

At the annual meeting of the Board, held in St. Louis on May 12, 1939, it was found necessary, on account of increased administrative expenses, to increase the application and examination fees. Effective May 12, 1939, these are as follows: application fee $15.00, payable on submission of application for review by board; examination fee $85.00, payable on notification to candidate of acceptance of the application and assignment to examination. Neither fee is returnable. This increase does not apply to candidates whose applications were filed prior to May 12, 1939.

For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, July 31

Tuesday, August 1

*10 a. m. - 12:30 p. m. Boston Dispensary tumor clinic.

Friday, August 4

*10 a. m. - 12:30 p. m. Boston Dispensary tumor clinic.

Saturday, August 5

*10 a. m. - 12 m. Staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Robert T. Monroe.

*Open to the medical profession.

August 30 - September 2 — Seminar in Physical Therapy. Page 857, issue of May 18.

September — Boston Psychoanalytic Institute. Page 450, issue of September 22, 1938.

September 4-6 — Institute for the Consideration of the Blood and Blood-Forming Organs. Page 941, issue of June 1.

September 4–6 — Institute at University of Wisconsin Medical School. Page 160.

September 5-8 — American Congress of Physical Therapy. Page 857, issue of May 18.

September 11-15 — American Congress on Obstetrics and Gynecology. Page 938, issue of December 8.

September 14-16 — Biological Photographic Association. Page 941, issue of June 1.

September 15-28 — Pan-Pacific Surgical Association. Page 863, issue of November 24.

October 23 - November 3 — New York Academy of Medicine. Page 977, issue of June 8.

Fall, 1939 — Temperature Symposium. Page 218, issue of February 2.

December 2 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

January 6, June 8–11, 1940 — American Board of Obstetrics and Gynecology. Page 160.

March 7–9, 1940 — The New England Hospital Association. Hotel Statler, Boston.

May 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

June 7–9, 1940 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

BOOK REVIEWS

Heart Patients: Their study and care. S. Calvin Smith. 166 pp. Philadelphia: Lea & Febiger, 1939. $2.00.

On opening this book one observes on the flyleaf that it is the fifth book which Dr. Smith has written on the subject of heart disease. Two of the previous books *How Is Your Heart* and *That Heart of Yours* were obviously written for lay consumption. The present volume according to the preface is for the benefit of "community practitioners." Since it is characterized throughout by a remarkable grammatical style, the reviewer may be forgiven for quoting *in extenso* directly from the book. The passages will also give an indication of the soundness of the factual content.

From the preface: "Looking backwards over a quarter of a century of heart specializing several outstanding truths glow on memory's horizon. They might be called the writer's Cardiac Aphorisms and their tenor dominates the pages herein. They include:

"1. The heart is more sinned against than sinning.

"2. Heart protests are not always heart disease.

"3. The muscle is of more importance than the murmur; the rhythm is of more importance than the rate.

"4. Heart, mind and spirit are inseparable companions in treatment.

"5. Effort, sustained and unremitting effort, of a physical, mental or emotional type, is the principal offender in depleting, disordering and disorganizing the heart and circulation."

Page 16: "Fatigue that regularly recurs at the close of each day is profoundly indicative of heart muscle weakness and cannot be dismissed with a gesture of inconsequence. The heart significance of fatigue is revealed by a first sound that is diminished in intensity and duration. These deficiencies are further reduced following an exercise test.

"Heart muscle fatigue may further be recognized by the fact that the tiredness or weariness is diffused generally all over the body, as twilight softly disseminates over a landscape."

Page 22: "Limitation on effort may take more profound ways of directing attention to the heart. For example, a spasm in a blood-vessel of a leg suddenly may inhibit walking, or both legs simultaneously may develop a weakness, a weariness and an insensibility to a degree where they cannot be used and the patient must rest or else fall. These two symptoms of spastic leg muscle contraction and leg insensibility are frequently among the first signs of myocardial damage."

Page 28: "People who are accustomed to living in mountain air or at high altitudes may fail to thrive and even develop circulatory faults at lower levels and in congested centers where the atmosphere is vitiated to some degree."

Page 57: "Cardiography is . . . the court of last resort in a differential diagnosis of heart conditions."

Page 57: "Cardiography differentiates between 'functional' and 'organic' heart trouble."

Page 141: "On cardioclinical examination the suspicion of syphilis will be aroused by arteries that are older than the years of the patient; also by a slow deliberate rate of 60 or less, with a sustained plateau at the wrist. A broad, heaving and displaced apical impulse may indicate syphilis, as also would an increase in the percussion diameter of the aortic arch.

"When there is a split first sound to the heart, the physician should bear in mind the possibility that syphilitic invasion of the heart's conduction system may be causing one ventricle to contract a fraction of a second later than its fellow of the opposite side. The suspicion of syphilis will also be aroused when the examiner hears a tinkling, musical or metallic sound over the base of the heart."

Page 141: "Heart patients have concealed and denied any earlier syphilitic invasion, only to confess reluctantly remote syphilis, when told that the heart behavior, or the cardiogram, points to the disease.

"Cardiography writes syphilis in bold, vigorous strokes."

With the final paragraph of the preface the reviewer finds himself in full agreement: "Should this volume prove of value in any heart emergency, or in any personal heart concern, to community practitioners, among whom I was one in the first ten years of practice and always in need of such a book, then shall its writing have been worthwhile."

Anemia in Practice: Pernicious anemia. William P. Murphy. 344 pp. Philadelphia and London: W. B. Saunders Co., 1939. $5.00.

Dr. Murphy has written a short monograph, which devotes the first 67 pages to the normocytic and hypochromic anemias and the remainder of the book to pernicious anemia. The numerous charts are well reproduced, and the colored plates are adequate. Certain of the illustrations, such as photographs of a microscope, blood-counting pipettes and icteric index standards, might be eliminated. On the whole, however, there is made available a considerable amount of useful information. The bibliography, while sufficient for the average practitioner, is by no means complete. There is a good index.

Pulmonary Tuberculosis: A synopsis. Jacob Segal. 150 pp. New York, London, Toronto: Oxford University Press, 1939. $2.75.

This book is a short outline of the present-day concepts of the diagnosis and treatment of pulmonary tuberculosis. One chapter deals with the prevention of this disease.

It is not a textbook for the beginner, neither is it a reference work for the practitioner. Out of one hundred and forty-eight pages, thirty-one are devoted to illustrations. Detail has been definitely sacrificed for the sake of brevity.

On the whole, the author has been very successful in giving the pertinent points in a very readable and delightful style, which at times leaves the reader somewhat in the dark. Only one paragraph is devoted to empyema complicating artificial pneumothorax therapy. A statement like, "Hard work or work which involves the inhalation of stone or metal dust or injurious gases" is a contributory cause in the development of tuberculosis, certainly needs further elucidation.

While former works have been too voluminous and bulky, this one leans a bit too far in the opposite direction. However the practitioner looking for a *short* outline on the present-day developments in the diagnosis and treatment of pulmonary tuberculosis will find it quite authoritative and up to date.

Biology for Pharmaceutical Students and Others. S. Mangham and A. R. Hockley. 613 pp. Baltimore: William Wood & Co., 1938. $6.50.

This book is a welcome and worthy addition to those already available on the subject. The arrangement and presentation of the material is excellent. The many illustrations are clear and will probably stimulate students to go beyond this stage of diagrams and by means of personal observation and dissection prove to themselves the author's incontrovertible statement: "Biology is not an armchair subject."

Nearly two thirds of the book are devoted to the consideration of the fundamental principles — morphological, chemical and physical — of plants. The textual approach to the various plants is very satisfactorily carried out.

The section on zoology is introduced by a discussion of the fundamental properties of life and the organization of the vertebrate body. Using the frog and the rabbit as types the student is introduced to the gross anatomy of the various systems of the body. The chapter on animal histology is adequate for the purpose, yet it might be made more useful by adding additional pages on organology. The study of the invertebrates centers about the ameba and paramecium, the hydra, the earthworm and the cockroach. The final three chapters deal with the importance of parasitism, the development of the frog and chick and outlines of evolution, variation and heredity.

A Textbook of Neuro-Radiology. Cecil P. G. Wakeley and Alexander Orley. 336 pp. Baltimore: William Wood & Co., 1938. $8.00.

With the recent advances in neurology, a new point of view has been reached in regard to the value of radiology to this specialty. The addition of Lipiodol to our diagnostic agents has led to a new study of the nervous system by the x-ray. Similar advances have been made through the use of air injections for encephalography and ventriculography. The effects of brain tumors, moreover, on bony structures are now better understood and more easily visualized by the x-ray. A book covering this field is needed and the text on review attempts to fill this want.

The publication, however, is far from satisfactory. The authors, using the material largely collected at the West End Hospital for Nervous Diseases in London, have, in general, covered most of the field, but much of their work has been taken from the work of others. One feels the lack of a personal report on the various conditions described. There must be many series of x-ray examinations at other hospitals where the material is much more abundant and, therefore, of greater use in writing a textbook on the subject. There is a paucity of illustrations, and certain well-established conditions, such as rupture of the intervertebral disks, the diagnosis of which is usually confirmed by x-ray, are only slightly touched upon.

Sir Thomas Roddick: His work in medicine and public life. H. E. MacDermot. 160 pp. Toronto: The Macmillan Co. of Canada, Ltd., 1938. $2.00.

Sir Thomas Roddick (1846–1923), one of the outstanding physicians of Canada, was largely responsible for introducing Lister's antiseptic methods into the Montreal General Hospital. As early as 1869, A. E. Malloch, who had served as a house surgeon at the Glasgow Royal Infirmary under Lister, reported some cases, as did Robert Craik, of Montreal. This work was disregarded, and it was not until 1877 that Roddick began to use the antiseptic method in Montreal. In two years, whatever skepticism there had been was almost entirely removed.

Roddick was also responsible for uniform medical registration in Canada; his bill, coming into force in 1912, provided for the Medical Council in Canada. The council grants a diploma giving the right to practice in Canada.

Dr. MacDermot, a medical historian of note, has written a delightful short life of Roddick. The book should be widely read by all American physicians as a medical biography of the first importance.

William B. Wherry, Bacteriologist. Martin Fischer. 293 pp. Springfield, Illinois and Baltimore: Charles C Thomas, 1938. $4.00.

Professor Martin Fischer's complete record of the life of William B. Wherry should be welcome to all men of science. The exact rendering of this life story is all absorbing and stirring. When one has finished reading this book, one has the distinct feeling that here is just the sort of man who should have his portraits reproduced and his achievements recounted. The book is well printed, beautifully bound and contains seventeen portraits. In addition there is a list of eighty-two publications at the end of the book, which constitutes the bibliography. It is a memorable book.

What It Means to Be a Doctor. Dwight Anderson. 87 pp. New York: Public Relations Bureau, Medical Society of the State of New York, 1939. $1.00.

Here are eighty-five "inspired" pages. Hippocrates and Osler are harked back to, fee-splitting is glossed over, the generosity of the profession is emphasized and the conventional questionnaire is used, all in the best tradition of the professional secretary. The name of the Association of American Medical Colleges is misstated, and there are other suggestions that it is the work of a tract writer. The only reference provided is to another publication of the same origin. The reviewer was unable to resist speculation concerning, and was somewhat annoyed by, references to a recent president of the American Medical Association. As propaganda for organized medicine it is legitimate, but organized medicine could get along without it.